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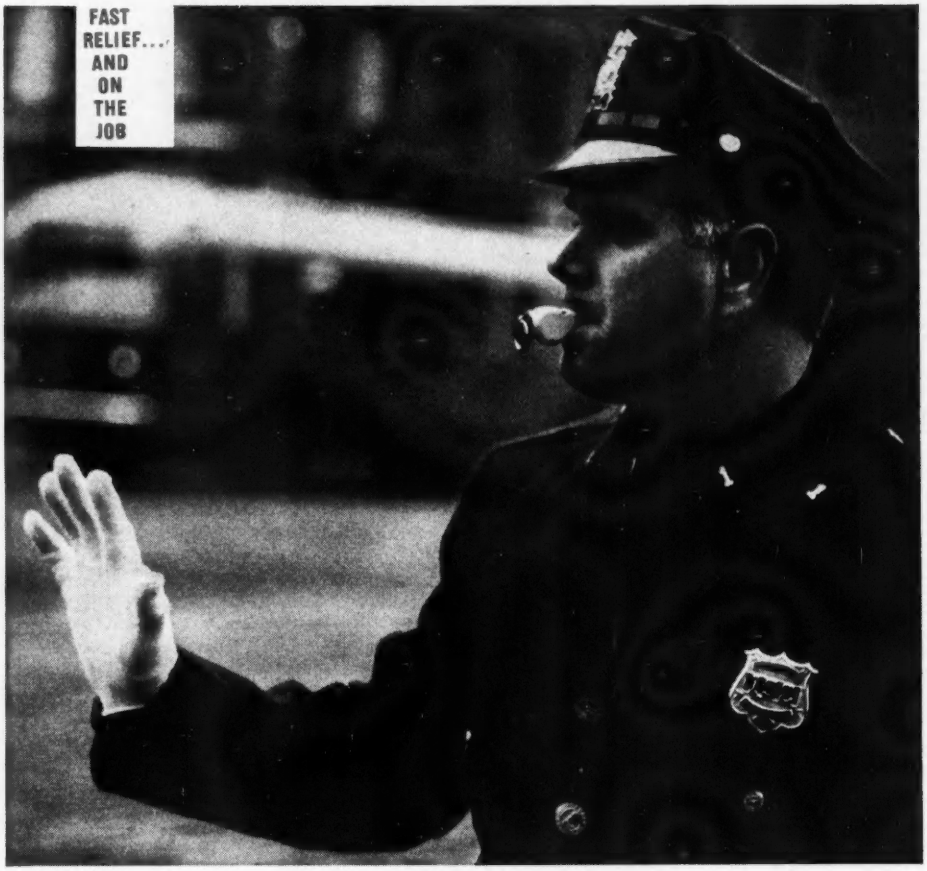

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The Treatment of Urinary Tract Calculi

WYLAND F. LEADBETTER, M.D., Boston

• From review of recent information relative to calculus formation in the kidney, the conclusion reached that we do not yet understand, despite much effort, the basic physicochemical mechanisms involved. Since this is so, it has seemed best to the author for the present to rely, in treating patients with renal stones, on simple therapeutic concepts, which, if carefully and conscientiously applied, produce good results. The concepts are the elimination of known causes such as parathyroid adenomas and obstructive lesions, elimination or at least treatment of infections, diminution of urinary components which form the basis of calculi by limiting the oral intake or absorption from the gastrointestinal tract and maintenance of a dilute urine of desired pH.

A plan for preoperative study is suggested to allow planned therapy. Indications for operative removal of calculi as well as some points of technique are discussed. It is emphasized that surgical removal of a calculus is but an incident in the care of patients with calculi and that treatment during the postoperative period and follow-up therapy is most important if success is to be achieved. Reports of cases to illustrate the application of these concepts are presented.

THERE IS A GREAT DEAL in the medical literature relative to factors in the initiation and development of urinary calculi, but it is safe to say that we do not yet know exactly how or why stones form. We recognize the relationship of excessive vitamin D administration, hyperparathyroidism, cystinuria and hyperuricuria to the development of calcium phosphate, cystine and uric acid stones and have assumed that such stones are to some extent the result of excessive concentration of these substances in the urine in association with inadequate volume of urine and urinary pH which favors the precipitation of crystals. Calculi developing in persons suddenly immobilized because of poliomyelitis, spinal injury or major trauma of any sort have been considered to result from high excretion of calcium salts released from the bony skeleton in association with inadequate volume of urine and high urinary pH.

There is no doubt that some stones form in the presence of obstruction and in the absence of demonstrable metabolic abnormalities by virtue, perhaps, of retention of crystals or crystalline masses which, in the absence of obstruction, would pass. Triple phosphate calculi occur frequently in the presence of urea-splitting infections, particularly when stasis is present as well.

We do not yet know much about oxalate metabolism and its relation to oxalate calculi. Nor do we know the specific factors responsible for the development of Randall's plaques in or on the surface of renal pyramids which act as the point of origin of some calculi.

It seems unlikely that in this country vitamin A deficiency, a demonstrated cause of experimental calculi in animals, can play a major role in stone formation. Little is yet known of the role of colloids

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in the process of stone formation. It has been assumed in the past that the physical state of dispersion of colloids may increase or decrease the ability of urine to hold the less soluble electrolytes in solution by adsorption. This may not be so.

Boyce, Garvey and Norfleet[2,3] isolated the urinary biocolloids (their term for urinary colloids) and found that they consist of at least two mucoproteins. The largest single component is a carbohydrate-protein complex of high molecular weight. These mucoproteins were found to be greatly increased in the urine of some patients with calcium calculi. Two patients with hyperparathyroidism had the highest concentration of any patients they studied. Boyce suggested that the organic matrix of calculi may be a modified or activated form of the mucoproteins normally found in urine. His concept of stone formation is that the initial and essential phase is a condensation of mucopolysaccharides and mucoprotein molecules constituting a coagulum of uncalcified matrix which may vary in size from a few molecules to a mass large enough to fill a renal calyx or pelvis. Deposition of inorganic crystals is a secondary phenomenon usually occurring quite rapidly but sometimes requiring weeks to reach maximum density in large calculi. The deposition of crystals is governed by the principles of physical chemistry which controls the formation of crystals from complex solutions. The origin of calculus matrix remains unknown but the presence of similar or identical mucopolysaccharides in connective tissue and in bone matrix has been demonstrated. The stone matrix could be derived from bone matrix or connective tissue outside the urinary tract.

Baker and Connelly[1] expressed the opinion that the high molecular weight of mucoproteins in the urine makes it unreasonable to assume that their presence in the urine is the result of filtration throughout the glomerulus or of secretion or excretion by tubule cells. In experimental work they demonstrated alterations in the renal tubule connective tissue mucoprotein immediately preceding the development of calculi in rats. This was observed consistently with four different methods of producing experimental renal calculi. Needle biopsy specimens of both kidneys were obtained from a small number of patients with unilateral calculi, and bilateral alterations of the renal tubule connective tissue matrix or mucoprotein were observed. In rats renal calcification or stone formation occurred in the altered mucoprotein whether within the kidney (nephrocalcinosis) or the renal pelvis or urinary bladder. As a result of these and other observations it was their impression that formation of urinary calculi may not be a disease of urine but rather a systemic condition specifically involving the renal connective tissue matrix of both kidneys. Baker expressed belief that evidence is accumulating that pathological calcification anywhere, including renal calculi, is a disease of connective tissue matrix and as such is essentially a collagen disease.

He went on to say that on the basis of this evidence—that is, altered connective tissue mucoprotein—he used "anti-inflammatory" drugs in treatment of animals with a known incidence of calculi and in a study of patients with recurrent stone, and there was an almost 50 per cent reduction of recurrence. Drugs used were acetylsalicylic acid, cortisone acetate, other corticosteroid hormones, phenylbutazone, and corticotropin. He cited the work of Snapper, Bendien and Polak,[8] who showed that sodium salicylate inhibits precipitation of urinary colloids, and concluded that this concept of salicylate action is more tenable than the assumption of Prien and Walker[5,6] that the administration of salicylate increases the solubility of calcium by virtue of increased glucuronide excretion in the urine.

Confirmation of these concepts is not yet at hand. Butts' use of hyaluronidase to increase dispersion of urinary colloids has not been substantiated. Prien's results from the use of acetylsalicylic or allied drugs to increase the solubility of calcium salts by the increased excretion of urinary glucuronides are open to question, although possibly their effectiveness may be found to be due to other mechanisms. The effect of estrogen and the role of citric acid as a calcium solubilizer has not yet been exploited.

We are left, therefore, with the necessity of dealing with factors that are to some extent under our control—metabolic disturbances, ingestion of calcium and phosphorus, urine volumes, urinary pH, obstructions and infections.

Since we are unable to single out potential stone-formers in the general population, we are not able to talk of the prevention of calculi except as we treat urinary tract infection, relieve obstruction and oversee the care of immobilized patients. We are, in general, confronted with the problem of preventing recurrence of calculi in persons relieved of calculi by spontaneous passage, cystoscopic instrumentation or operation. We also may be called upon to try to prevent further growth of calculi known to be present but for some reason not removed and, in addition, to try to dissolve them. So far, the methods available have been disappointing.

It is the purpose of this paper to show that effective therapy is possible without reference to colloids or acetylsalicylic acid.

It has been my observation that, in general, little is to be accomplished by attempts at dissolution or

limiting the growth of calculi. Most patients ultimately require surgical operation because of an acute situation due either to infection or obstruction or both, which not infrequently leads to operation at a time when removal of the stone is more difficult and necessary reparative procedures less likely to bring about a good anatomical and physiological result. It seems best to state that, barring exceptional situations resulting from age or serious disease, all calculi should be removed in appropriate fashion and at an appropriate time. The treatment of patients with renal or ureteral stones should be divided into three parts: (1) Preoperative examination, observation and treatment, (2) cystoscopic or operative removal and (3) postoperative care.

As a basis for postoperative therapy to prevent regrowth of calculi, complete examination and observation before operation is essential. It has become my practice to study all patients fully, regardless of the apparent situation. Sometimes this is impossible before operation because of an acute situation, but, if so, it should be done as soon as possible after operation because unexpected information may emerge from the study. The necessity for this has been impressed upon me in the course of treating patients with unrecognized hyperparathyroidism, hyperuricuria, cystinuria, and obstructive inflammatory situations which led to unnecessary sacrifice of kidneys, unnecessary disability, expense, and even death.

The plan for study of a patient consists of:

1. A careful history with emphasis on past and present urinary tract symptoms, injuries, operations, treatment of gastric or duodenal ulcer, dietary habits, usual daily fluid ingestion. Often this discloses valuable information which may permit a shrewd guess as to some factors responsible for calculi.

2. Physical examination, which is often unrewarding but should nevertheless be done carefully. Occasionally one may palpate a parathyroid nodule, or upon examination of the kidney areas, abdomen, genitalia or prostate, abnormalities may be noted which require investigation and may have causative relationship.

3. Examination of the urine. This should include a careful study of the sediment with attention to the crystalline content which may give a good lead as to the type of calculus. Culture and sensitivity studies provide a basis for antibiotic therapy before and after operation. The presence of urea splitting organisms should be known. A nitroprusside test for the presence of cystine should be routine. A Sulkowitch test for calcium provides a rough idea of the calcium content in the urine.

4. X-ray studies are initiated with a kidney-ureter-bladder film and intravenous urograms, which may provide all necessary information, including the probable composition of calculi. However, in my opinion cystoscopic examination is essential. This should include estimation of residual urine, study for ureteral reflux, observation for bladder neck obstruction, and bilateral ureteral catheterization for collection of urine specimens for culture and estimation of pH. Good pyeloureterograms are essential. I have noted that ureterograms are often inadequate or often not done. An air pyelogram may be helpful in distinguishing nonopaque calculi from tumors of the renal pelvis or ureter. If calcium stones have been repeatedly found in one kidney, it is a good plan to get differential calcium excretion studies because occasionally the kidney in which stones reform may be found to excrete more calcium than its normal mate.

5. Blood is always drawn for serum calcium and phosphorus estimation as well as for uric acid determination. It is important to know these values. Since the determination of calcium in the laboratory is one of the more difficult tests, one must know with certainty what the normal values for each laboratory are. Otherwise, the diagnosis of hyperparathyroidism, which is essentially based on laboratory findings, is impossible. It is my custom to also collect 24-hour urine specimens for determination of calcium excretion, preferably with the patient on a normal diet, since this represents normal conditions; but if calcium excretion is considerably elevated, the patient may be given a low calcium diet for two days before the test is repeated. Determination of 24-hour excretion of uric acid may be desirable if the patient has uric acid stones, since this forms the basis for estimating the magnitude of the problem and may provide a good guide as to the effectiveness of therapy.

When these tests and examinations have been completed, one knows a great deal about the case. Negative results of tests are as valuable as positive ones. It is desirable, in the presence of hyperparathyroidism, not to operate for the removal of calculi until the parathyroid tumor is removed because of the danger that calculi will quickly recur. Cystine or uric acid calculi should not be removed until the urine has been made alkaline. It is a good plan to keep a chart of the pH of each voiding for a day or two before operation to determine how much alkalization is necessary.

CYSTOSCOPIC AND OPERATIVE REMOVAL OF CALCULI

Instrumental removal of ureteral calculi is a valuable procedure but it calls for judgment and skill and is not without hazard. In general, one may

state that only small calculi in the lower third of the ureter should be dealt with in this manner. Very jagged calculi even though small, should probably be removed by open operation rather than risk significant trauma to the ureter which may lead to stricture. A urologist's choice of methods depends somewhat on experience and skill. My own method of procedure is to operatively remove all ureteral calculi which have lodged in the upper third of the ureter, to operatively remove large (greater than 0.8 cm. in diameter) calculi lodged in the lower ureter unless they are in the intramural portion and can be caused to pass by cystoscopic ureteral meatotomy. I make one attempt to by-pass small calculi by cystoscopic manipulation and to extract them with a catheter loop or Johnson-type stone basket constructed of nylon threads. If this is not successful but the calculus can be passed by several catheters, I sometimes leave the catheters in place and occasionally get a stone by twisting and removing the catheters later. Usually, however, and particularly if there is evidence of infection above the stone, ureterolithotomy is done without delay in order to avoid the likelihood of an established pyelonephritis. Free drainage of urine is the best treatment for acute pyelonephritis. Many times significant renal damage occurs as a result of repeated attempts to remove a stone by cystoscopic manipulation.

The surgical treatment of renal calculi should have as its purpose:

1. The complete removal of all calculi without permanently damaging the parenchyma, pelvis or ureter.

2. Correction of any obstructive lesion.

3. The removal, by partial nephrectomy, of any renal unit that is irreparably damaged, not needed, and in which recurrence of stone is likely. (This may not be feasible when all functioning renal tissue is necessary to support life.)

It is probable that in the conduct of renal operations for stone, few urologists successfully accomplish these aims regularly. As a result of incomplete removal, "recurrence" of stone often takes place. Of course, the removal of all stone fragments may be technically impossible without severely damaging the kidney. The lack of recognition of mild ureteropelvic junction obstruction or replacement of the ureter or ureteropelvic junction after operation in such a way that angulation or stricture develops, often leads to persistence of infection or recurrence of stone or both. In the course of operation the ureteropelvic junction and upper ureter should be carefully visualized and obstruction by stricture or anomalous vessel corrected. The need for surgical correction can usually be anticipated if proper preoperative study is conducted. Proper repositioning of the ureter and pelvis is often aided by nephropexy. Occasionally, the ureter or ureteropelvic junction must be maintained in proper position by the insertion of a catheter split through the cortex or the renal pelvis.

There is usually no great technical feat connected with the removal of a calculus or calculi free in the pelvis unless the pelvis is all or nearly all intrarenal. In such cases one can make the operation relatively easy by freeing the kidney completely, thus exposing the renal vessels, and by tipping the kidney in the best way to approach the pelvis, retract the renal vessels, and expose enough of the intrarenal pelvis to incise it safely by retracting, but not incising, the renal tissue overlying the pelvis, using a small vein retractor. There is no need for haste in such cases. A little time spent in exposing all structures makes for safety, for less trauma, and for less likelihood of subsequent stricture of the ureteropelvic junction. When the pelvis is large enough to allow it, a narrow retractor may be placed in the pelvis and give good visual exposure of all the pelvis proper, even allowing one to look into the various infundibula or major calyces.

When calyceal stones are present which may not be removed by way of the pelvis it has been my practice to put a bulldog clamp on the renal artery to prevent bleeding, to locate the stone by putting a finger into the pelvis, and then incise the renal capsule directly over the stone. Using the blunt handle of the knife, it is possible to separate the elements of the renal parenchyma and approach the stone directly through the renal pyramid. Since there is no bleeding to obscure the view, one may see into the calyx, particularly if a small nasal speculum is used to retract the renal parenchyma. Using this technique one may visualize crystals or small fragments of stone on the calyceal mucosa and remove them with small wipes of gauze.

Partial staghorn calculi may often be removed by pyelotomy if one takes time to gently dilate the neck of infundibula or calyces to allow the segments of stone found in these compartments of the pelvis to slip through. Such stones may be delivered by traction and rotation of the stone while pressure is applied on the surface of the kidney. Radial incisions from the hilum through the cortex, except very short ones, are to be decried, since branches of the renal artery supplying the anterior or posterior halves of the kidney may be divided.

I believe that large staghorn calculi or large calculi which may not be delivered through the pelvis should be removed by longitudinal incision

along the coronal plain (Brödel's line) after first occluding the renal artery. The incision should be made with reference to the location of the stone. Very rarely must the entire kidney be completely sectioned. The incision should be made through the renal capsule and then the renal tissue separated, using the knife handle. By this method renal vessels can be demonstrated and ligated as one approaches the pelvis. After removal of all stone and gently wiping the calyces and pelvis free of fragments, one may release the renal artery and clamp and ligate any bleeding vessels with fine sutures. The kidney pelvis and parenchyma may then be closed without using heavy sutures which will compress and destroy renal parenchyma.

The use of nephrostomy or pyelostomy tubes should, in general, be avoided since these almost inevitably lead to the introduction of organisms all too often of the urea-splitting variety. A small vent in the pelvis with a drain placed near it is all that is necessary, and this should be removed as soon as possible.

Altogether, it would seem that a major effort should be made to improve the nicety of intrarenal operations. Much may be accomplished by a reevaluation of this subject. When fluoroscopic visualization of the calyces, pelvis and ureter becomes possible and practical, and particularly when cinefluoroscopy is generally available, the information obtained can be expected to guide the surgical technique. Renal arteriography may be of great aid in planning the surgical removal of renal calculi.

POSTOPERATIVE CARE

After operation to remove calculi, which is often wrongly considered an end in itself, comes the problem of after-care. The immediate problems associated with this phase are rapid restoration of urine flow through the kidney for its flushing action to rid the kidney of clot, fibrin and crystalline debris. A high fluid intake is desirable unless there are limiting factors such as cardiac disease or pronounced renal impairment. A daily intake of at least 3,000 cc. of fluid, and preferably more, during the postoperative period is desirable. This accomplishes two things: It maintains a dilute urine in relation to electrolyte content and teaches the patient what an adequate fluid intake actually is in terms of fluid per day. It is not enough to urge patients to drink fluid; one must see to it that they do take adequate amounts.

In addition, one must stress around-the-clock administration of fluids for patients who are recurrent stone-formers. Adequate and appropriate antibiotic therapy is essential and should be based on sensitivity studies made on urine obtained for culture before operation or directly from the kidney pelvis at operation.

Patients with cystine or uric acid stones should be given enough 50 per cent sodium citrate solution by mouth to maintain an alkaline urine of pH 7 during the whole 24 hours. This may necessitate drinking the solution during the night. Charts should be kept of the pH of all voided urine until the proper alkalinization is accomplished. The patient should be encouraged to do this at home by himself so that one may know for sure whether the urine is maintained at the proper pH.

Patients with calcium stones and triple phosphate stones should be held to a low calcium diet, and administration of fluid should be pushed hard. If a complete removal of all but crystalline fragments of stone has been accomplished, the immediate postoperative period is very important, for it appears than in many patients recurrence of stone develops very early. A good acidifying agent aside from acid-ash diet is cranberry juice. It can be used liberally in place of other fruit juices. Perhaps all stone patients should be given acetylsalicylic acid or an equivalent, although this is far from being an established important therapeutic addition. In any case, it will do no harm.

After immediate convalescence has been accomplished an intravenous pyelography should be done to see what the functional and anatomical condition of the upper urinary tract is. If there is evidence of obstruction or residual calculi, then the operation was inadequate. It is best to know this early and to plan reoperation in cases in which it is necessary.

The necessity for long-term and careful observation, in the office, of patients who are recurrent stone-formers is obvious. This consists of interval radiographic study and careful examination of the urine to make sure it is crystal-free and of the proper pH. Patients with calcium oxalate stones usually do well by simply ingesting enough fluids. On the other hand, patients with recurrent calcium phosphate or triple phosphate stones are real problems. In addition to adequate fluid intake, which may necessitate a constant daily consumption of 4,000 cc., a low calcium diet obtained by eliminating dairy products from the diet and supporting therapy to immobilize calcium or phosphorus in the bowel may be tried. This should be controlled by estimation of calcium and phosphorus urine excretion for 24-hour periods before and during administration of medication to know whether it really is effective.

To approach this problem from the phosphate side, the use of the Shorr regimen[7] (aluminum jel preparations) in amounts of 3 or 4 ounces each day partially blocks the absorption of dietary phosphorus and may be of benefit, although it may cause troublesome constipation. Its use would seem

to be most indicated in the presence of triple phosphate stone. The elimination of part of the phosphate excreted in the urine might be expected to result in depriving calcium, magnesium and ammonium ions of phosphate radical to form insoluable triple phosphate. Recently, Henneman, Carroll and Albright[4] reported the use of sodium phytate to decrease the urinary excretion of calcium and magnesium. Their studies indicated that 9 gm. per day of sodium phytate taken by mouth considerably decreases absorption from the bowel and accordingly urinary excretion of calcium and magnesium. One-third to one-half of the administered phytate apparently is not absorbed. It probably forms insoluble and unabsorbable complexes with calcium and magnesium. As a consequence of decreased absorption, the urinary excretion of calcium and magnesium decreases without materially altering calcium balance, suggesting that the absorption of dietary calcium is blocked but that there is no interference with the resorption of calcium secreted into the intestine through the bile and other intestinal juices. These investigators concluded that sodium phytate appears to be a safe therapeutic agent in adults and of value in the treatment of certain renal stone syndromes. It would appear that this may offer a valuable addition to the treatment of patients with recurrent calcium phosphate and triple phosphate calculi. Further investigation is certainly warranted.

To illustrate a few of the problems of diagnosis, surgical treatment and postoperative care, the following cases are presented:

CASE 1. The patient, a 42-year-old physician, was admitted to hospital November 20, 1955. He gave a history of bilateral renal colic at intervals since 1947, often associated with hematuria and the passage of multiple small calculi. None of the calculi had been analyzed but uric acid crystals had been found in the urine. An intravenous urogram, made just before admittance to hospital, showed relatively nonopaque calculi in both kidneys with mild hydronephrosis on the left. There was a history of diabetes in the family but the patient himself had never tested his urine for sugar. The blood uric acid content was said to be normal.

On physical examination he was observed to be somewhat obese. The blood pressure was 145/95 mm. of mercury. Tenderness was noted in both costovertebral angles. The hemoglobin content was 14.6 gm. per 100 cc. of blood. Leukocytes numbered 9,450 per cu. mm. The urine had a strong acid reaction, specific gravity of 1.021, 2+ albumin and 1+ sugar content, and 50 erythrocytes and 5 leukocytes per high power field. Culture of the urine showed Staphylococcus aureus sensitive to chloramphenicol. A nitroprusside test on the urine was negative for cystine. Serum content of calcium was 9.6 mg., of phosphorus 3.4 gm., and of uric acid

Figure 1 (Case 1).—Intravenous urogram. This demonstrates mild bilateral hydronephrosis, filling defects in renal pelves due to calculi, and good function of each kidney.

7.2 mg. per 100 cc. Calcium excretion in the urine (the patient not being on a low calcium diet) was 49 mg. in 24 hours. Phenolsulphonphthalein excretion was 35 per cent in one-half hour, 88 per cent in two hours. Fasting blood sugar at the time of admission was 163 mg. per 100 cc., but when a glucose tolerance test was done the blood sugar went from 176 mg. to 385 mg. per 100 cc. in two hours.

Results of x-ray studies were as follows: The chest was normal. A kidney-ureter-bladder film showed bilateral renal calculi filling the renal pelvis The stones were only semi-opaque and suggested either cystine or uric acid content. Both kidneys excreted contrast substance promptly. There was bilateral hydronephrosis of about equal degree. The ureters were not dilated (Figure 1).

Removal of the calculi was planned after the urine was made alkaline by oral administration of 50 per cent sodium citrate solution. It was found it was necessary to give 8 cc. of this solution four times a day to bring the pH of the urine up to 7. No insulin was given before operation.

The left kidney was operated upon on November 25, 1955. The incision was placed over the 12th rib, which was subperiostially resected. The kidney appeared somewhat scarred but the ureter was not dilated. The pelvis was found to be largely intrarenal and crossed by an anomalous artery and vein passing to the lower pole of the kidney. By retracting these with a small vein retractor the pelvis was satisfactorily exposed so that a longitudinal incision could be made. The stone was found to be triangu-

lar. By careful freeing, the stone was finally delivered without injury to the vessels, the pelvis or the kidney. Palpation of the interior of the pelvis then revealed many small calculi in the lower and middle calyces. Most of them were extracted by the finger, but one calculus in the lower calyx and another in the mid-calyx had to be removed through small nephrotomy incisions made directly through the renal pyramids. As almost no bleeding occurred it was not necessary to place sutures in the renal parenchyma or capsule. A nephrostomy tube (whistle-tip No. 28 Latex catheter) was placed through the lower nephrotomy into the pelvis so that urine could be obtained directly from the pelvis for microscopic study and pH determinations.

Convalescence from operation was very satisfactory. Urine from the nephrostomy tube was clear and was maintained at a pH of 6.5 to 7. On December 1, dye was injected through the nephrostomy tube and a pyelo-ureterogram was obtained which showed no residual calculi or obstruction. The nephrostomy tube was removed. Because of some wound infection, evidence of spillage of sugar in the urine, and elevated blood sugar, administration of protamine zinc insulin, 15 units each morning, was begun. The wound infection cleared and on December 12, 1955, the large triangular stone and several smaller stones were removed from the right kidney by anterior pyelotomy. Since there was no bleeding and no evidence of obstruction, the pelvis was closed except for a small vent and the wound drained with a rubber wick. Following this there was some fever for several days due to pulmonary atelectasis, which gradually cleared. Urine never drained from the incision. The rubber drain was removed on the seventh postoperative day. An intravenous urogram (Figure 2) showed good function without evidence of hydronephrosis. Upon analysis the stones were found to be pure uric acid.

The patient was sent home with prescription of fluid intake of 4,000 cc. daily, 8 cc. of 50 per cent sodium citrate solution to be taken four times a day, the last just before retiring (this having been found to maintain the urine at a pH of 7), diabetic diet without insulin, and instructions to have the urine cultured after two weeks, and to take additional antibiotics (chloramphenicol) if any infection persisted.

The patient followed all instructions completely. The latest report was on March 23, 1957, and at that time the urine was sterile. Intravenous pyelograms showed no abnormality, the urine was kept free of uric acid crystals by maintaining a fluid intake of 4,000 cc. a day and the continued use of alkalizing agent. The patient had found that two teaspoonfuls of 50 per cent sodium citrate solution four times a day maintained the urine at a pH of 7 at all times. The blood urea nitrogen content 12 to 17 mg. per 100 cc. and to uric acid content was between 4.5 and 5.1 mg. per 100 cc. The Diabetes was controlled.

Note: This case illustrates the successful handling

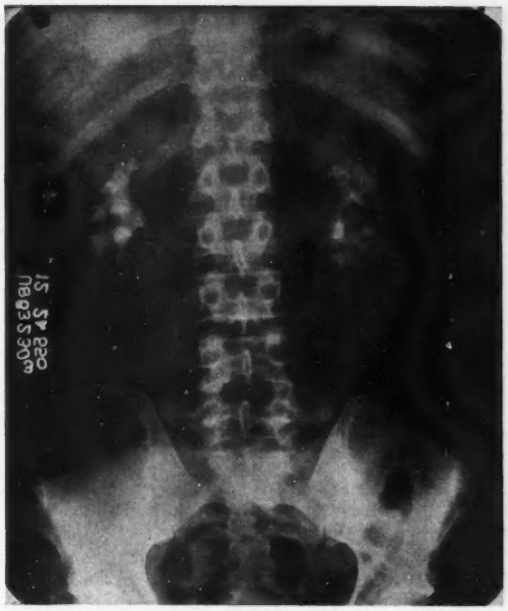

Figure 2 (Case 1).—Postoperative intravenous urogram which demonstrates almost complete resolution of bilateral hydronephrosis. No residual calculi are demonstrated.

of a complicated uric acid stone problem with complete cooperation of the patient and gives details of the examination, observation and tests, the preoperative preparation, the operative removal of calculi and the postoperative care necessary in dealing with such a case.

CASE 2. The patient was an 18-year-old college student admitted first to the Phillips House of the Massachusetts General Hospital on January 23, 1955. He gave a history of having had bladder calculi removed at the age of two and of right nephrectomy for calculus disease at the age of ten. None of the calculi were analyzed.

In August, 1954, a relatively nonopaque stone was demonstrated by x-ray in the remaining kidney. At the same time it was found that the serum uric acid was elevated to 9 mg. per 100 cc. The serum calcium and phosphorus content were within normal limits. The patient was placed on a weight reducing regimen and a low purine diet. Fluids were forced. In spite of these measures the stone increased in size and in density. It was removed in December 1954 at another hospital. Stone analysis at that time showed calcium oxalate. The patient was then admitted to the Massachusetts General Hospital for study, having made a good convalescence from the operation.

Except for multiple surgical scars and mild obesity, no abnormalities were noted on physical examination. The blood pressure was 130/90 mm. of mercury. The urine gave an acid reaction, the specific gravity was 1.022, the albumin reaction 1+.

It contained cystine crystals. Staphylococcus albus reasonably sensitive to chloramphenicol grew on a culture of urine. The serum uric acid content was 6.8 mg. per 100 cc., calcium 9.2 mg. per 100 cc., and phosphorus 3.7 mg. per 100 cc. Urine calcium excretion in 24 hours was 104 mg. Phenolsulphonphthalein excretion was 30 per cent in one-half hour and 80 per cent in two hours. An intravenous urogram showed no calculi. The left kidney shadow appeared somewhat enlarged. The kidney excreted dye promptly and in good concentration. The calyces appeared somewhat blunted and the lower infundibulum slightly widened. There was no evidence of ureteral obstruction, however (Figure 3).

Neither the mother nor the father of the patient had cystinuria. It was obvious that cystinuria and formation of cystine stones was probably the primary problem in this case and that the calcium oxalate in previous stones was owing to the secondary deposition of calcium oxalate on a cystine nucleus. The patient was discharged with instructions to take three to four thousand cubic centimeters of fluid daily, to omit dairy products from his diet and to take 12 cc. of 50 per cent sodium citrate solution four times daily. He was taught how to determine the urinary pH and specific gravity and how to examine the urinary sediment for crystals. To do this, he bought a microscope. He was to keep charts so that we could study the effectiveness of the therapy.

All went well for a time. The urine remained at a pH of approximately 7.5. Fluid intake approached 4 liters daily. X-ray films showed no recurrence of stone until January of 1956 when a kidney-ureter-bladder study demonstrated a calculus again in the kidney. It seemed that the precipitating factor was an automobile trip to Mexico in the fall of 1955, during which the patient strayed from the prescribed regimen. As a consequence he was readmitted to the Massachusetts General Hospital on February 20, 1956.

The blood pressure at this time was 100/70 mm. of mercury. An intravenous urogram showed a clearly defined calcification, consisting of a partial staghorn stone filling the lower calyces and the lower infundibulum of the remaining kidney (Figure 4). Renal function was prompt and, except for distortion of the lower calyces by calculus, the pelvis and the calyces appeared essentially normal. Laboratory studies showed serum uric acid of 7.2 mg. per 100 cc., calcium 104 mg. per 100 cc. and phosphorus 4.1 mg. per 100 cc. Urinary calcium excretion in 24 hours was 61.2 mg. on one occasion and 127.6 on another. The urine was again positive for cystine (nitroprusside test).

It was felt that the stone should be removed before it became larger and more of a surgical problem. Therefore on February 27 the left kidney was explored and the stone removed through a pyelotomy and a small nephrolithotomy. It was found that there were two types of stones, an irregular rough stone which was found to consist of calcium phosphate and cystine, and small spherical stones consisting of pure cystine. At operation a nephrostomy tube was left in the pelvis through the lower calyx for four days. A renal biopsy showed a normal kidney. Convalescence was entirely satisfactory.

Figure 3 (Case 2).—Intravenous urogram. There is good renal function with slight dilatation of all calyces.

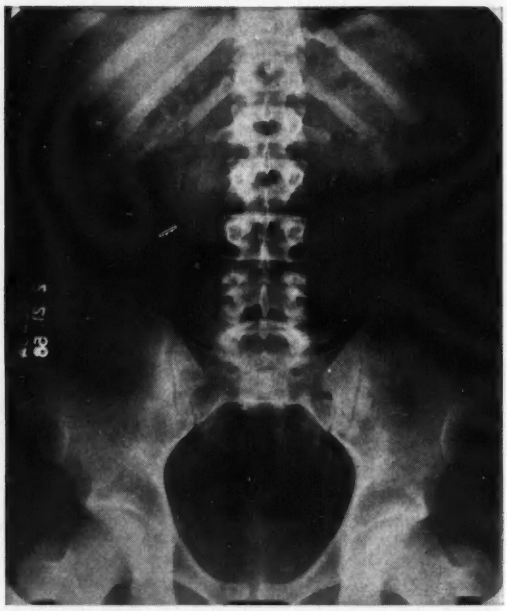

Figure 4 (Case 2).—Kidney-ureter-bladder x-ray film. The calculus filling the lower calyces and infundibulum is clearly shown.

Figure 5 (Case 2).—Postoperative intravenous urogram. Although the dye obscures them here, two small residual calculi were noted on the kidney-ureter-bladder film.

Figure 6 (Case 2).—Retrograde pyelogram made 10 months after operation. Subsequent pyelographic studies in July 1957, 16 months after operation, showed no calculi and similar pyelographic picture.

Urine obtained directly from the left kidney pelvis at operation was sterile. Phenolsulphonphthalein excretion was 70 per cent in two hours. A postoperative intravenous urogram (Figure 5) showed two probable small residual or recurrent nonopaque calculi in the lower calyces of the kidney. There was no change in the calyceal pattern but there was a suggestion of narrowing of the uretero-pelvic junction, thought probably due to postoperative scar. It was hoped that this would resolve.

It seemed quite certain at this point that cystine calculi represented the primary problem, which was compounded by the deposition of calcium phosphate due to the maintenance of an alkaline urine. Study of the urine sediment showed that cystine crystals appeared when the pH was below 6. Calcium phosphate crystals became apparent above pH of 7. The problem therefore was a difficult one. It was finally decided to try to maintain a mildly alkaline urine with low specific gravity by a high fluid intake and a moderate dose of 50 per cent sodium citrate daily. In addition, acetylsalicylic acid was given in the hope that the drug might favorably affect the solubility of calcium phosphate in the urine.

The patient was readmitted for study on December 27, 1956. He had no complaints of any sort. Cystoscopy and calibration of the left ureter were carried out. The ureter took a No. 10 bulb easily, but 10 cc. of urine could be aspirated from the kidney pelvis, indicating inadequate drainage. A kidney-ureter-bladder x-ray film and air and conventional pyelograms were made. The small stones that had been visualized ten months before were less clearly visualized, but there seemed to be still one or more small stones in the lowest calyx. Moderate dilatation of the calyces and pelvis was still present (Figure 6). The patient was discharged with instruction to continue the regimen as before, and he continued well. Intravenous urograms made in July, 1957, showed no calculi.

Note: It may be desirable in this case to resect the lower calyx as a stone-bearing area, since calculi have not demonstrably formed elsewhere in the kidney. It would seem possible that the two operations on the lower calyces damaged the calyceal musculature so that peristaltic activity of these lower calyces is not normal. In any case, this illustrates one of the more difficult stone problems—primary cystine stones associated with calcium oxalate or calcium phosphate stones probably due to alkalinization of the urine with decreased solubility of calcium and a tendency to precipitate on cystine nuclei. A regimen of alkalinization and high fluid intake, to be fairly effective must be rigidly adhered to, regardless of other considerations. It is fortunate that the patient here reported upon is intelligent, willing and cooperative. The complexity of the problem in handling such cases is well illustrated. Fortunately, infection was of no major concern in this case.

Case 3. A 60-year-old woman was admitted to the Phillips House of the Massachusetts General Hospital on October 30, 1950. At that time she gave a history of bilateral flank pain since the age of 5

Figure 7 (Case 3).—Kidney-ureter-bladder x-ray film. This demonstrates large and smaller calculi filling the left renal pelvis, and multiple small calculi in a decidedly hydronephrotic right kidney.

Figure 8 (Case 3).—Intravenous urogram delineates normal upper left calyces, dilated and distorted lower left calyces. There is almost no dye excreted by the right kidney.

years. The nature of her trouble was not discovered during childhood. In 1934 she passed a calculus. More recently a kidney-ureter-bladder x-ray film was made which showed calcified shadows in the region of the right kidney. Pyuria was also demonstrated. An examination in 1950 revealed exophthalmos, a symmetrically enlarged thyroid gland, blood pressure of 180/90 mm. of mercury, evidence of arteriosclerosis and tenderness in the left flank. There were many leukocytes in the urine. Culture of a specimen of urine grew E. coli. The nonprotein nitrogen content of the blood was 26 mg. per 100 cc. The serum calcium was 9.6 mg. per 100 cc. and the phosphorus content 3.6 mg. per 100 cc. Cystoscopy was done and a catheter was passed to the left pelvis, from which 180 cc. of clear urine was drained. On the right a catheter would not enter the pelvis. Retrograde pyelograms were poor but did demonstrate obstructions in both uretero-pelvic regions. It seemed likely that numerous calcified shadows in the right abdomen were calculi in a decidedly hydronephrotic right kidney. A Finney-type pyeloplasty was done on the left side on November 29, 1950. Satisfactory convalescence followed.

On February 15, 1953, the patient was readmitted with myocardial infarction, from which she made a slow but satisfactory recovery. She was then well until March 9, 1956, when she began to have severe pain in the left flank and oliguria. This was followed some hours later by copious output of urine containing much gravel. X-ray studies were obtained which showed a large staghorn calculus occupying the left kidney pelvis and calyces (Figure 7). The stones in the right kidney area were as previously noted. An intravenous pyelogram showed fairly prompt excretion on the left side, outlining dilated calyces (Figure 8). The uretero-pelvic junction was not visualized. At this point I was asked to see the patient. Cystoscopy was carried out and the bladder was observed to be inflamed. The left ureter was catheterized but the catheter would not pass through into the kidney pelvis. A retrograde pyelogram (Figure 9) demonstrated narrowing of the left uretero-pelvic junction. Laboratory studies showed pronounced pyuria. The urine culture showed nonhemolytic streptococci and B. coli sensitive to chloramphenicol, terramycin, aureomycin and tetracycline. The nonprotein-nitrogen content was 24 mg. per 100 cc. of serum. Serum uric acid was 5.9 mg., calcium 9 mg. and phosphorus 3.2 mg. per 100 cc. Urinary calcium excretion in 24 hours was 364 mg., which perhaps was due to the abundance of calcium phosphate shed from the stones into the urine.

It was obvious that, since the right kidney was asymptomatic and almost functionless, operation on the left to remove the calculi and correct the uretero-pelvic obstruction was obligatory. This was carried out on April 11, 1956. At operation the kidney appeared scarred but the cortex was not greatly thinned. An anomalous artery and vein were found crossing the uretero-pelvic junction embedded in scar tissue. The uretero-pelvic junction itself was considerably narrowed. It was obvious that the anomalous vessels had to be divided in order to carry out any type of operation. The stones were

Figure 9 (Case 3).—A left retrograde pyelogram which demonstrates stricture at the left ureteropelvic junction and filling of pelvis and calyces about calculi.

Figure 10 (Case 3).—Intravenous urogram made before discharge of patient, demonstrating good function, diminished hydronephrosis and funneled uretero-pelvic junction.

removed through an anterior pyelotomy and two small nephrotomy incisions. The lower part of the kidney which had been rendered ischemic by division of the anomalous vessels was resected. Correction of the uretero-pelvic junction obstruction was carried out by resecting the area of stricture, excising a portion of the redundant pelvis, and reimplanting the ureter into the pelvis in an oblique fashion—in other words, using the principle of elliptical anastomosis. A splinting latex rubber ureterostomy catheter was placed through the lower infundibulum and down the ureter. The pelvis was drained by a whistle-tip nephrostomy tube passed alongside the ureteral splint.

Convalescence was very satisfactory. During the first 24 hours, 1,500 cc. of urine was collected from the left nephrostomy tube. It was found that when fluid was injected into the nephrostomy tube, it passed quickly to the bladder. The kidney pelvis was irrigated daily, using a continuous drip of solution G* through the nephrostomy tube until April 21, when the tubes were both removed. On this date a kidney-ureter-bladder x-ray film and a pyelogram were obtained by injecting contrast medium through the nephrostomy tube. This revealed no evidence of residual calculi. The pelvis was small and funneled and it drained quickly via the ureter. During this time a daily output of 2,000 cc. was maintained. The patient was given supplementary therapy of acid-ash, low calcium diet and cranberry juice to help acidify the urine, Basaljel (basic aluminum carbonate gel), 30 cc. four times a day, and appropriate antibiotics. Urinary pH charts showed that the urine was maintained at a pH of between 5 and 6. Urinary excretion of calcium before the patient was discharged was 65 mg. and of phosphorus 230 mg. in 24 hours.

An intravenous urogram (Figure 10) showed very satisfactory function of the left kidney with absence of the stones previously noted, a decrease in the degree of hydronephrosis and prompt emptying. The right kidney remained unchanged. Intravenous urograms were repeated in July, 1956, and in March, 1957, and showed no recurrence of stones in the left kidney or evidence of uretero-pelvic junction obstruction (Figures 11 and 12).

The patient was discharged with prescription of a low calcium, acid-ash diet supplemented by cranberry juice and 3,000 cc. of water daily. Three grams of acetylsalicylic acid and 4 ounces of Basaljel a day were also advised. She followed that regimen until the time of this report, except the Basaljel was discontinued after six months because of pronounced constipation. The urine remained infected but specimens contained only a few leukocytes. The patient was asymptomatic. The urinary pH stayed between 5 and 6.

Note: This case illustrates stone formation in relation to obstruction and infection, and shows that careful removal of calculi together with reconstructive operation and a good postoperative pro-

*Magnesium oxide 15.2 gm., anhydrous sodium carbonate 17.6 gm., citric acid 129.2 gm., distilled water to make 4,000 cc.

Figure 11 (Case 3).—Kidney-ureter-bladder x-ray film taken after one year. No recurrence of calculi is noted.

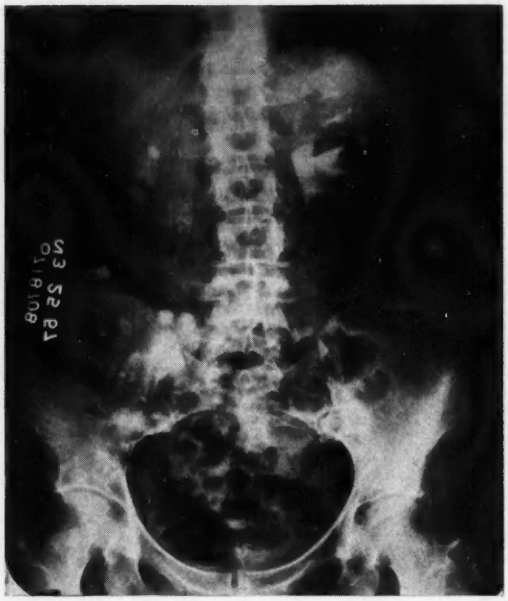

Figure 12 (Case 3).—Intravenous [illegible] after one year, showing further diminution of left hydronephrosis.

gram of free drainage, fluids, diet and medication have much to offer for cases of this type. It was most fortunate that the patient did not have an active urea-splitting infection to combat as well.

CASE 4. A 69-year-old woman was admitted to the Massachusetts General Hospital on November 11, 1956. The history was one of repeated episodes of urinary lithiasis beginning 20 years before when a stone had been removed by cystoscopic manipulation. Eleven years before, the right kidney had been removed because of calculus disease. An impacted left ureteral stone was removed by ureterolithotomy in August, 1956. Up to that time no stone analyses or serum calcium or phosphorus studies had been carried out. During the convalescence from the ureterolithotomy, stones were noted to have recurred in the left kidney. Serum calcium was found to be 12 mg. per cent and the patient was referred to me for study. She had never had a dietary or medical regimen prescribed.

On physical examination the patient appeared to be healthy. The blood pressure was 188/100 mm. of mercury. The thyroid was normal to palpation. Abdominal scars were noted and the left kidney was somewhat tender.

The urine showed a specific gravity of 1.011. It was neutral with 4+ albumin, contained no sugar, but had many leukocytes and erythrocytes. Coliform bacilli not sensitive to any drug except neomycin grew on a culture of urine. Nonprotein nitrogen was 25 mg. per 100 cc., uric acid 6.6 mg., fasting blood sugar 99 mg. and total protein 7 gm. per 100 cc. (albumin 4.2 gm., albumen 2.8 gm.).

Figure 13 (Case 4).—Kidney-ureter-bladder x-ray film showing recurrent calculi in remaining kidney.

Phenolsulphonphthalein excretion was 15 per cent in a half hour and 43 per cent in two hours. Serum calcium was 12.6 mg. per 100 cc. on one occasion and 12.2 mg. on another. The phosphorus content was 2.2 mg. and 2.8 mg. per 100 cc. Urinary calcium excretion was 197 and 273 mg. in 24 hours.

Figure 14 (Case 4).—Intravenous urogram. Obstruction of infundibula by calculi has caused moderate calyectasis.

Figure 15 (Case 4).—Pyelogram obtained by injecting nephrostomy tubes illustrates method of splinting ureteropelvic junction and draining kidney.

X-ray films of the chest and bones showed no abnormality. Barium swallow films showed indentation on the right side of the esophagus compatible with parathyroid adenoma. A kidney-ureter-bladder roentgenogram and intravenous urogram which the patient had had in an outside hospital (Figures 13 and 14) showed multiple calculi filling the lower half of a bifid left kidney pelvis with considerable hydronephrosis of the upper half. Seven to ten stones were visualized, the largest being about 2 cm. in diameter. A diagnosis (presumptive) of hyperparathyroidism, renal calculi and chronic pyelonephritis of the remaining kidney was made. The surgical consultant agreed. It was decided to explore for a parathyroid adenoma and subsequently to operate to remove stones from the left kidney. Exploration was carried out December 1, 1956, and an adenoma (pathologically proved) was found within the right lobe of the thyroid. Convalescence was satisfactory. Serum calcium was 7.6 mg. per 100 cc. immediately after operation and later was 8.9 mg., 8 mg. and 9.4 mg. per 100 cc., the last on December 18, 1956. Serum phosphorus on these occasions was 3.6, 3.2, 3.1, 4.2 and 6 mg. per 100 cc. No supplementary calcium was given.

It was felt by the medical consultant that the urinary calculi remaining in the left kidney might disintegrate or pass, but it seemed to me, in view of the solitary kidney, and significant infection, if such occurred, it might be extremely hazardous since it was more than likely that stone fragments would obstruct, necessitating emergency procedures with the likelihood of more renal damage. Therefore, on December 11, 1956, the left kidney was explored.

Figure 16 (Case 4).—Intravenous urogram before discharge of patient. This shows prompt function and resolution of hydronephrosis.

It was found that the extrarenal pelvis was very tiny and divided just above the uretero-pelvic junction into upper and lower infundibula which were moderately strictured. The stones were removed by pyelotomy, except for several small calculi in the

lower calyces which were removed through a small nephrotomy incision in the lower pole. After all calculi were delivered it was found that the ureteropelvic junction had been traumatized badly. Therefore two ureteral splinting catheters as well as two nephrostomy tubes were introduced to maintain drainage from both halves of the kidney in the immediate postoperative period. One splint-catheter and one nephrostomy tube were introduced through the nephrotomy incision which had been made previously to remove the calculi, and the other ureterostomy tube and nephrostomy tube were introduced through one of the upper calyces to provide drainage from the upper half of the kidney. The patient tolerated the operation well in spite of the fact that the calyces behind the stones were filled with pus. A pyeloureterogram obtained by injecting contrast medium into the nephrostomy tubes several days later (Figure 15) illustrates the method of drainage. All tubes were removed 16 days after operation when the pelvis was filled with dye and no leakage of it occurred at the uretero-pelvic junction.

An intravenous urogram (Figure 16) was made on December 31, 1956, just before discharge from the hospital, which showed moderately good function and reasonably free drainage. No calculi were visualized. During the postoperative period no special therapeutic measures were used other than the maintenance of a high fluid intake and the use of an acid-ash diet with cranberry juice to help maintain an acid urine. Last reports from the physician who had referred her were that patient was free from urinary complaints. There were no pus cells in the urine and the pH was maintained at from 5.5 to 6. Intravenous urograms showed no calculi or obstruction at the uretero-pelvic junction.

Stone analysis showed ammonium and calcium phosphate and oxalate.

Note: This case illustrates the not uncommon history of patients with renal calculi due to parathyroid adenoma. Repeated colic, often several operations and frequently the loss of one kidney may occur before the diagnosis is made—which suggests that, in the presence of calcium stones, serum calcium and phosphorus studies should always be made.

Massachusetts General Hospital, Boston 14.

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Social Security Footnotes

TO SUPPORT socialistic practices in regard to retirement funds requires that, for the sake of consistency, socialized medicine also be supported. If one believes that the federal government should tax everyone to provide an income for each upon retirement or disability, one must also believe that the same government should, with equal propriety, tax everyone to provide medical care for all!

—From the Department of Public Relations, American Medical Association

Cerebral Vascular Diseases

Certain Clinical and Electroencephalographic Aspects

RICHARD D. WALTER, M.D., and HARRY FANG, M.D., Los Angeles

• In a preliminary study of 52 patients with cerebral vascular disease, clinical and electroencephalographic evaluations were compared. Most of the patients were in the sixth and seventh decade of life and had had symptoms of cerebral vascular disease for over a year. Seventeen of the patients had clinical evidence of intermittent cerebral ischemia. When routine electroencephalographic techniques were used, 47 per cent of the records were within normal limits. Twenty patients with cerebral vascular disease, eight of whom had clinical cerebral vascular insufficiency, were studied during posturally induced hypotension. No activation was detected in any of these 20 patients. It would appear that other methods of activation, including tilt-table studies, and serial recordings should be further explored and evaluated in these disorders if more clinically useful information is to be gained.

INCREASING INTEREST in cerebral vascular disease has developed in the last several years, owing in part to the trial of newer therapies and the appreciation that many of the clinical problems in these disorders are still unsolved. Electroencephalography has been widely used in neurology, psychiatry and general medicine as a diagnostic aid, and its use has been extended to the study of vascular disease of the cerebrum. The consensus has been that the electroencephalogram has not been particularly helpful clinically in such conditions, most investigators reporting the tracings are within normal limits in 40 to 50 per cent of cases of cerebral vascular disease.[1,2,4,10,12,13] These reports, however, expressed the average, based on routine recordings regardless of the clinical stage of the disease. Some attempts have been made to increase the amount of information from electroencephalographic study by using activating techniques such as sleep, photic stimulation and compression of the carotid artery.[7,9,11] Interest has also grown in the clinical and electroencephalographic features of cerebral vascular insufficiency or transient ischemic attacks. Meyer, Leiderman and Denny-Brown[8] reported on the use of a posturally induced decrease in systemic blood pressure to elicit focal electroencephalographic changes.

The present preliminary report on a long term clinical and electrophysiological study of patients with cerebral vascular diseases is a joint undertaking of the University of California at Los Angeles Medical Center and the Veterans Administration Medical Center, Los Angeles. Routine electroencephalograms were made in all cases and in a smaller group of patients investigations with posturally induced hypotension were carried out.

MATERIALS AND METHODS

Fifty-two patients with a history of cerebral vascular disease who resided at the Domiciliary Home of the Veterans Administration Medical Center were studied. The majority were not in need of hospital care and were ambulatory. Each patient was examined one or more times by one of us (Fang) and a comprehensive medical and neurological history was obtained. The evaluation included a neurological and physical examination, a review of available records, x-ray films of the skull, electrocardiographic and electroencephalographic tracings, blood sugar and cholesterol determination and other selected procedures as indicated. A diagnostic impression of each case was formulated. The routine electroencephalogram included an assay of the major scalp areas both by scalp-to-scalp and scalp-to-ear techniques, along with a period of overbreathing when possible. These records were interpreted without knowledge of the clinical diagnosis of the individual patient.

Twenty patients were selected for study on the tilt-table. Some patients with a history of intermittent ischemic episodes were included in this group. For this study, the patient was placed on a manually operated tilt-table. Electroencephalographic recordings were obtained with a scalp-to-scalp technique and a continous lead 1 electrocardiogram was recorded on one channel. Blood pressure determinations were made frequently and any clinical observations or subjective sensations were recorded. After a control period in the horizontal position, the

From the University of California at Los Angeles Medical Center, Department of Medicine (Neurology), and U. S. Veterans Administration Center, Los Angeles.

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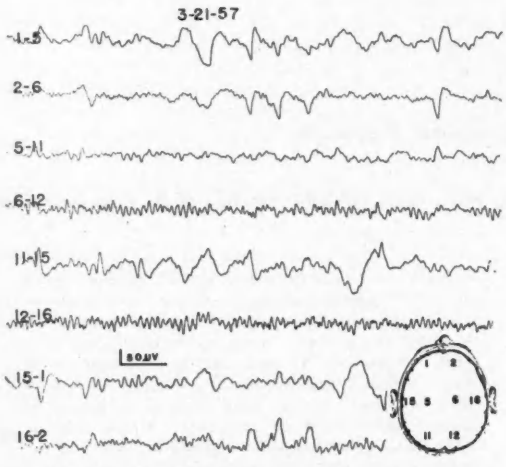

Figure 1.—A sample electroencephalogram demonstrating focal, slow (1 to 3 cycles per second) activity over the posterior aspects of the left hemisphere. (Electrodes 11-15.)

patient was tilted head up to 70 degrees. At least five tilts were done in each case, the first change of position being done gradually over 25 to 30 seconds, then succeeding tilts with increasing rapidity, the last one being within a 5-second period. For each tilt the patient was held at the 70 degree angle for approximately 2 minutes or until a decrease in blood pressure was detected. The patient was then returned to horizontal and several minutes elapsed between each tilt. In one case, opportunity was afforded to make serial routine recordings during the course and development of a thrombosis of the internal carotid artery.

ANALYSIS OF CLINICAL DATA

The age of patients ranged from the fourth to ninth decades of life; the largest group was composed of those in the seventh decade. The mean average age was 62.7 years. All the 52 patients in the study were male veterans. Arterial hypertension was noted in 17 cases. Evidence of inadequacy of peripheral arterial pulsations was present in nearly two-thirds of the cases. Atherosclerosis of the cerebral arteries was then the presumed common etiological factor. Roentgenographic evidence of intracranial calcifications along the course of internal carotid arteries in the cavernous sinus was demonstrable in at least 20 cases. Definitely asymmetrical or unequal carotid pulsations were noted in 13 cases on careful digital palpation along the course of the vessels in the neck. Bilateral, symmetrical reduction in the amplitude of carotid pulsations could be palpated in six instances in the neck. Retinal arteriolar blanching following gentle digital compression of the optic bulb on direct fundoscopy was evoked in six cases. Twelve patients in this study group had had episodes of convulsive seizures, either preceding, during or following the cerebral vascular attacks. Ten persons gave a history of syncopal attacks (with loss of consciousness associated with retrograde amnesia) at the onset of cerebral vascular episodes. The length of time since the first occurrence of vascular lesions in these cases, as determined by the history of symptoms referable to cerebral vascular events, ranged from ten months to 33 years. Three patients had had strokes between ten months to one year before the time of this study, 20 patients two to five years before, 15 patients six to ten years before and nine from 11 to 33 years before. Some of the patients had had but one isolated event with permanent residual effect and others up to five or ten transient episodes with almost complete functional recovery.

ELECTROENCEPHALOGRAPHIC DATA

The routine electroencephalograms were within normal limits in 24 (47 per cent) of the 52 cases, and 28 or 53 per cent were clearly abnormal. Little in the way of subtle or relatively minor abnormalities were noted. Of the 28 abnormal records, 24 showed focal abnormalities consisting of slow 1 to 3 cycles per second (cps) or 4 to 9 cps activity. No spiking activity was observed. Two of the abnormal records were diffusely slow and two records showed paroxysmal activity. The majority of the focal records consisted of slowing over the anterior portions of the hemisphere; four had lateralized slowing and three showed slow wave activity over the posterior aspects of the hemisphere. The typical electroencephalographic findings are shown in Figure 1.

The following is a report of the electroencephalographic changes that were observed during the course of a thrombosis of the internal carotid artery:

CASE 1. A 49-year-old man was admitted to the hospital with history of intermittent weakness and loss of control of the right arm for about ten days. On the day before admission, transient periods of aphasia and some paresthesia of the right hand had developed.

Upon examination, in addition to the mild weakness of the right hand, he was found to have diminished carotid pulsation on the left. Figure 2 is a section of the electroencephalogram on the day of admission, showing mild focal changes with 5 to 7 cps activity over the anterior temporal and frontal regions on the left. An arteriogram was performed to evaluate the left carotid system. However, before the procedure was carried out it was noted that the patient was aphasic and had profound hemiplegia on the right. The arteriogram showed an obstruction at the origin of the left internal carotid artery. An

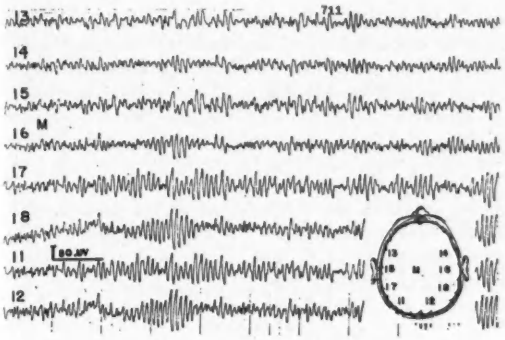

Figure 2.—A very slight irregularity and some rare, slow (5 to 7 cycles per second) activity is present over the temporal region on the left. (Electrodes 13 and 15.)

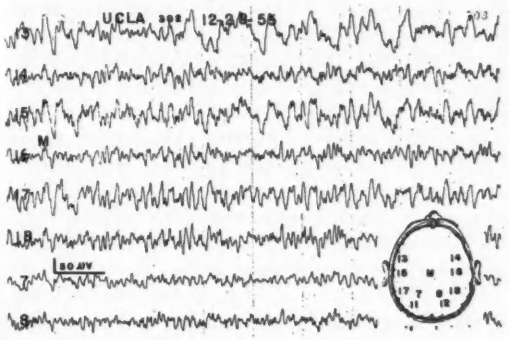

Figure 3.—There is a prominent, slow wave focus of 1 to 3 cycles per second waves over the left temporal region. (Electrodes 13 and 15.)

emblectomy was done and an old thrombosis with a more recent extension was found. A slight retrograde flow was obtained. Subsequent electroencephalograms demonstrated the persistence of focal and generalized slowing (Figure 3). When examined three months later, the patient had only slight improvement of aphasia.

CORRELATION OF CLINICAL AND ELECTROENCEPHALOGRAPHIC DATA

Although 12 patients had definite convulsive phenomena clinically, only two records were paroxysmal in type. Ten patients also had syncopal attacks. This lack of agreement between clinical convulsive episode and the electroencephalogram is somewhat higher than that encountered in patients with convulsive disorder without cerebral vascular disease. Schwab[10] also noted this poor correlation on routine studies of patients with cerebral vascular disease and recommended the use of serial recordings and of activation techniques.

As to which side was affected by the lesion, clinical findings and electroencephalographic abnormality were in agreement in all but two of the cases in which electrical abnormality was shown. In these two, clinical signs were bilateral. All of the patients with intermittent ischemic episodes had normal routine electroencephalograms (which emphasizes the need for a suitable activating technique). Of the two patients with clinically diagnosed basilar insufficiency, one had a normal encephalographic tracing and the other had a tracing demonstrating anterior focal abnormality. Fifteen patients had one or both signs compatible with involvement of the carotid system. They had either a blanching of the retinal arteries on digital compression or diminished or absent pulsation of the carotid arteries on one or both sides. Eight of these patients had electroencephalographic demonstration of focal abnormality.

Seventeen patients had hypertension and six of the 17 had normal electroencephalograms while 11 had abnormal tracings. One tracing was diffusely slow, two had generalized slowing with paroxysmal features, three had both focal abnormality and diffuse slowing, and five exhibited focal slowing. This would seem to indicate a fairly high degree of electrical abnormality associated with hypertension and cerebral vascular disease.

RESULTS OF TILT-TABLE STUDIES

The results of the tilt-table studies—done in 20 cases—were not particularly revealing. Patients with normal electroencephalographic records in the horizontal position did not have abnormal tracings when the 70 degree tilt was carried out. In patients with abnormal records in the horizontal position, neither increase in over-all slowing nor extension of a focus was noted when the tilting studies were done. Figure 4 illustrates a normal electrical pattern before, during and after the tilt. Blood pressure changes were noted in nearly every case when the tilting was done, the maximum decrease being 56 mm. (mercury) systolic and 20 mm. diastolic, although the average decrease was considerably less. Several patients described dizziness during the tilting procedure but there was no concomitant electrical change. In this group of 20 patients, two had basilar-vertebral disease, one had bilateral carotid disease, one had combined carotid and basilar insufficiency, and four had unilateral carotid disease. The remaining twelve were classified as having infarctions—one or more—of more fixed or chronic type. The following case is presented as an example of insufficiency of the basilar-vertebral type.

CASE 2. A 46-year-old former policeman gave a history of suddenly having a pulling sensation of the hair over the scalp while he was lying down to rest. He promptly lost consciousness and knew nothing of events of the next 11 days. Upon exam-

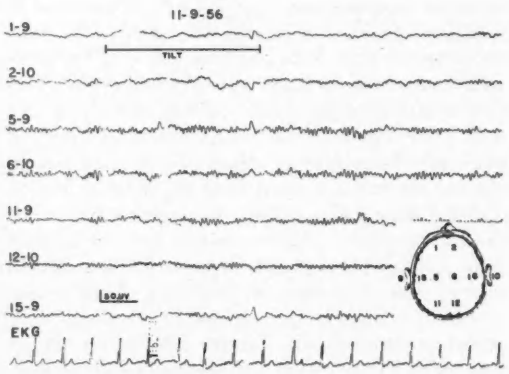

Figure 4.—An electroencephalogram recorded during the tilting procedure with simultaneous lead 1 electrocardiogram on the last channel. There are no decided abnormalities in the record.

ination, weakness on the left side and numbness involving the right side of the body were noted. He was put in a hospital in Michigan for nine months and recovered. Some three months before the episode of unconsciousness he had had transient blurring of vision lasting for 45 minutes as well as a tingling sensation over the left little finger. He said that after recovery from the period of unconsciousness he had noted similar tingling sensations now and again involving all four fingers of the right hand. Upon examination, a moderate degree of emotional lability was noted. Also observed were jerky conjugate sweep movements of the eyes, hemi-anesthesia and analgesia over the left half of the face, a deviation of the palate to the right, left central facial weakness, weakness of the left masseter muscle, spastic left hemiplegia, hyperactive deep tendon reflexes on the left, a left extensor plantar response and left hemi-analgesia and hypoesthesia.

The following is a short report of a case of internal carotid artery disease.

CASE 3. The patient, a 52-year-old man, had a series of cerebral vascular episodes involving the right side of the body over a five-year period. While having dinner, he was suddenly unable to hold his cup with his right hand. In the course of a few minutes, he became totally paralyzed on the right side of his body without any alteration in awareness. He was also unable to speak, and he noticed numbness over the right extremities. Six weeks later the ability to speak returned and strength was restored to the right leg and right arm. A year later, without warning, the right-sided weakness returned but without disturbance of speech. Again considerable improvement occurred over a few weeks. Some three years after the first episode, the patient woke with complete right-sided paralysis and global aphasia. Numbness over the entire right half of the body returned. At that time the patient had had hypertension for about ten years.

Upon examination, a reduction in carotid pulsation on the left side of the neck was noted. Digital compression over the optic bulb on the left brought about immediate blanching of the retinal arterioles as observed on direct fundoscopy, but not on the right side. Other abnormalities were a low-pitched, slurred speech, slight impairment of recall for remote events, right central facial weakness, residual spastic right hemiparesis, hyperactive deep tendon reflexes most pronounced on the right, with a right extensor plantar response. There was no objective evidence of sensory loss.

DISCUSSION

Although in this group of patients there was considerable variation as to the site and degree of involvement as well as the duration of the illness, there was a great predominance of patients in whom the cerebral vascular disease was of more than a year's duration. The chronic nature of the illness in these patients should be considered in the interpretation of the results of the study. The electroencephalographic findings on routine examination are in keeping with those reported by other investigators. In most reported series, electroencephalographic abnormalities in between 40 and 50 per cent of cases of cerebral vascular disease was noted, but most series include more acute material. There is a high degree of agreement, as might be expected, between the electroencephalographic and the clinical evidence as to which side of the brain is involved. Yet nearly 50 per cent of the routine records in cases of known cerebral vascular disease are within normal limits. The factors involved in the production of electrical abnormality are probably the site of the disease, the vessel involved, the depth of the lesion, the degree of occlusion, the extent of the colateral circulation and the stage of the process. Some of these factors have been investigated in experimental work with animals, but in the area of clinical practice many details are lacking. Factors opposing the detection of electrical abnormality probably include the inability to explore nearly 80 per cent of the cortex, the intermittent nature of abnormality (it may be missed on one examination), and a lack of gradation between normal and abnormal cerebral tissue. Dead neurons do not produce electrical activity.

Meyer and co-workers[8] reported the appearance of focal slowing over the posterior scalp areas in cases of insufficiency of basilar-vertebral type and central focal slowing in carotid insufficiency. Although the series herein reported on contained eight patients who clinically appeared to have intermittent cerebral ischemia, no electrical abnormalities were activated. Even so, it would appear too early to abandon the use of this technique for the study of cerebral vascular insufficiency. From this preliminary

study it would appear that other methods of activation might be explored, as well as the use of serial recordings for the detection of electrical abnormality in some cases of cerebral vascular disease.

University of California at Los Angeles School of Medicine, Los Angeles 24 (Walter).

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Hyperthyroidism

Diagnosis by Failure of Triiodothyronine to Suppress Uptake of Iodine[131]

LEO SMOLLAR, *M.D.*, San Diego

• **Sixty patients with abnormally high I^{131} uptake were treated with liothyronine (L-triiodothyronine) for seven or eight days and then tested again. Fifty-five patients showed a suppression of iodine uptake sufficient to eliminate the possibility of hyperthyroidism. Also the therapeutic trial of liothyronine indicated whether they were euthyroid, or hypothyroid with iodine deficiency. Six of the patients showed insignificant change in the I^{131} uptake after treatment with thyroid hormone—that is, the change from the original uptake was less than 30 per cent. These six patients were later confirmed to be hyperthyroid. In four patients the uptake at the second test was less by between 35 and 52 per cent than at the first. These four patients, like the remainder with even greater suppression in thyroid uptake, remained clinically euthyroid.**

The repeat I^{131} uptake test was thus seen to be considerably more accurate than the single test and well worth the time required to perform it.

THE I^{131} (radioactive iodine) uptake test measures the amount of iodine taken up by the thyroid gland and thus is also a measure of thyroid activity. The I^{131} test is uncomplicated: A known amount of radioactive iodine is ingested by the patient and the amount taken up by the thyroid gland is measured by means of a scintillation counter. Abnormal uptake is an indication of thyroidal disorders. Werner,[4] Perlmutter,[3] and McConahey and Owen,[2] among others, have suggested, however, that the diagnostic value of the test can be increased if it is repeated after the patient has received the thyroid hormone.

The principle of the uptake depression test is that the normal thyroid gland is inhibited by the thyroid hormone, while the hyperactive gland is affected only slightly or not at all. Perlmutter[3] reported that "a decrease of more than 30 per cent of the initial iodine uptake following the ingestion of thyroid hormone is almost universally indicative of the

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TABLE 1.—*Response of Hyperthyroid Patients to I^{131} Uptake Tests*

Case No.*	Age and Sex	Uptake (Per Cent) Before Liothyronine: In 6 Hr.	Uptake (Per Cent) Before Liothyronine: In 24 Hr.	Uptake After Liothyronine: In 6 Hr. (Per Cent of Dose)	Uptake After Liothyronine: Per Cent Change From First Test	Uptake After Liothyronine: In 24 Hr. (Per Cent of Dose)	Uptake After Liothyronine: Per Cent Change From First Test
6	51 M	31	68	49	+63	70	+ 3
11	44 F	30	42	28	— 7	40	— 5
15	42 F	30	46	32	+ 7	48	+ 4
16†	24 F	22	33	18	—18	25	—24
47	55 F	79	88	69	—13	85	— 3
60	68 M	47	65	48	+ 2	68	+ 5

*Numbering of cases agrees with numbers in Table 3.

†This patient is listed here although the original uptake was not clearly in hyperthyroid range. Thyroidectomy had been done three years before. Symptoms had recurred and a scintigram indicated about eight grams of functional thyroid. Uptake of I^{131} was suppressed only 24 per cent. She responded satisfactorily to I^{131} therapy.

TABLE 2.—*Response of "Doubtful" Patients to I^{131} Uptake Test*

Case No.*	Age and Sex	Uptake (Per Cent of Dose) Before Liothyronine: In 6 Hr.	Uptake (Per Cent of Dose) Before Liothyronine: In 24 Hr.	Uptake (Per Cent of Dose) After Liothyronine: In 6 Hr.	Change (Per Cent)	Uptake (Per Cent of Dose) After Liothyronine: In 24 Hr.	Per Cent Change From First Test
13	26 M	25	45	17	—32	26	—42
17	18 F	28	46	16	—45	29	—37
54	19 F	48	64	18	—62	31	—52
55	54 F	34	60	20	—41	35	—42

*Numbering of cases agrees with numbers in Table 3.

euthyroid state." Such a change occurred in 95 per cent of euthyroid patients and in only 3 per cent of hyperthyroid patients examined by him.

This presentation deals with a study that was carried out to evaluate the uptake depression test of thyroid activity in order to determine the general usefulness of the test and whether it is sufficiently accurate to justify the time and effort it demands.

TABLE 3.—*Response of 61 Patients with Abnormally High Uptake of I^{131} to Second I^{131} Test*

Case No.	Age and Sex	Per Cent of Dose of I^{131} Taken Up				Reduction of 24 Hr. Uptake (Per Cent)	Protein-Bound Iodine After Thyroid Hormone (Micrograms per 100 cc.)
		Before Liothyronine		After Liothyronine			
		In 6 Hr.	In 24 Hr.	In 6 Hr.	In 24 Hr.		
1	41 F	30	40	8	7	82	5.5
2	26 F	25	43	3	3	93	5.9
3	23 F	26	39	6	3	92	8.1
4	40 F	28	42	11	10	76	5.1
5	33 F	27	44	11	12	73	4.4
6	51 M	31	68	49	70	No depression	9.0*
7	33 F	29	49	10	10	80	5.6
8	20 F	23	38	7	6	84	5.5
9	32 F	57	69	10	10	86	6.3
10	34 F	28	43	7	5	88	5.1
11	44 F	30	42	28	40	5	9.0*
12	23 F	20	44	14	12	73	5.7
13	26 M	25	45	17	26	42	6.4
14	60 F	21	50	8	7	86	6.0
15	42 F	30	46	32	48	No depression	6.0*
16	24 F	22	33	18	25	24	....*
17	18 F	28	46	16	29	37	7.1
18	55 F	35	55	8	8	85	7.1
19	34 F	26	44	6	4	91	6.0
20	30 F	42	49	9	12	76	....
21	19 F	26	43	7	8	81	....
22	13 F	31	45	12	11	75	5.4
23	17 F	25	47	6	8	83	6.1
24	60 F	37	55	4	6	89	5.6
25	68 F	30	47	6	8	83	....
26	36 F	31	51	7	3	94	....
27	58 F	26	44	6	8	82	....
28	30 F	22	41	8	15	63	5.7
29	33 F	25	56	4	3	95	5.3
30	41 F	36	50	7	9	82	5.5
31	35 F	22	40	5	3	93	4.9
32	26 F	31	45	7	6	87	6.3
33	30 F	24	40	9	8	80	6.3
34	34 F	33	51	9	11	78	5.1
35	26 F	26	41	5	3	93	5.0
36	40 F	26	51	11	12	76	5.8
37	17 F	21	45	6	6	87	....
38	53 M	21	46	8	7	85	....
39	45 F	36	52	4	4	92	....
40	32 F	26	47	6	5	90	6.1
41	46 M	47	67	4	3	55	....
42	50 F	21	42	10	9	79	6.0
43	31 F	25	39	5	5	87	....
44	44 F	33	55	8	10	82	6.1
45	25 F	39	66	9	14	79	....
46	17 F	29	44	6	10	77	....
47	55 F	79	88	69	85	3	....*
48	26 F	30	53	4	3	43	7.4
49	30 F	27	52	4	3	42	5.2
50	44 F	31	52	7	7	87	5.2
51	33 F	40	58	14	15	74	4.3
52	28 F	30	46	16	22	52	5.5
53	47 F	37	51	9	8	84	5.7
54	19 F	48	64	18	31	52	....
55	54 F	34	60	20	35	41	....
56	41 F	36	57	17	28	51	....
57	36 F	25	42	12	13	69	....
58	43 F	36	49	8	7	86	5.5
59	30 F	27	48	10	10	79	7.4
60	68 M	47	65	48	69	No depression	7.1*
61	55 F	25	43	10	12	72	5.0

*Hyperthyroid patient.

Of 518 men and women tested for thyroidal disorders, 96 patients (18.5 per cent) were found to have abnormally high uptake of I^{131}. Sixty of these patients were given a second I^{131} uptake test after they had taken 75 micrograms of liothyronine (L-triiodothyronine) daily for seven or eight days. Liothyronine was used in preference to desiccated thyroid or thyroxin because it acts more promptly. Desiccated thyroid would have had to be given for two or three weeks.

Before the second test each patient was carefully examined for signs of symptomatic improvement and for possible side effects to medication. Usually protein-bound iodine determination was done.

RESULTS

Of the 60 patients with high uptake of I^{131} who were given liothyronine, 51 showed decided decrease in uptake (at the second test it was less than 30 per cent of the original level). Clinical course and further laboratory studies confirmed that none of the subjects were hyperthyroid.

In four patients, the uptake at the second test was between 48 per cent and 70 per cent of the original level. These were classified as "doubtful," but later clinical course proved them all euthyroid.

The remaining five patients (Table 1) showed either an increase in uptake or suppression of less than 30 per cent, and were therefore considered hyperthyroid. The protein-bound iodine was high in two of these patients, not high in two and not done in one. Subsequent observation, together with the response to therapy, confirmed the diagnosis of hyperthyroidism in all five.

One of the four patients classified as "doubtful" (suppression of uptake was less than 52 per cent but more than 30 per cent) was a teenage girl with a diffuse goiter of about 40 grams which gradually disappeared under therapy with 75 micrograms of liothyronine daily. This is patient No. 3 on Table 2. The four "doubtful" patients are now considered euthyroid after a year's observation.

The diagnosis of hyperthyroidism from observation of a high uptake of I^{131} by the thyroid gland is rendered considerably more accurate by a demonstration that the uptake is not depressed more than 30 per cent by the taking of 75 micrograms of liothyronine a day for eight days. Hypothyroidism that is masked by a high uptake of I^{131} may also be brought to light by giving this drug, for it relieves the patient's symptoms. The greater reliability reduces the need for additional laboratory studies to confirm the diagnosis and decreases the possibility that antithyroid therapy will be given unnecessarily.

The repeat I^{131} uptake test has still another advantage: The interval of administration of thyroid hormone permits the physician to distinguish between patients who have hypothyroidism with a high uptake of I^{131} and those who are hyperthyroid or euthyroid. If, for example, a patient has an iodine deficiency goiter with hypothyroidism, a trial with liothyronine will suppress the high I^{131} uptake and will usually make him feel much better. The decrease in I^{131} uptake distinguishes him from hyperthyroid patients, while the clinical improvement sets him apart from euthyroid persons, who rarely feel any effect when given liothyronine.

All things considered, the only disadvantage to doing a second I^{131} uptake test after an interval of administration of thyroid hormone is that it adds to the diagnostic time.

Table 3 shows the results of the double I^{131} uptake tests on all 61 patients.

2454 Third Avenue, San Diego 1.

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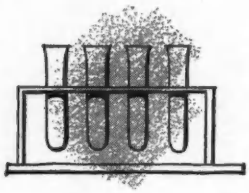

Dysfunctional Uterine Bleeding

The Relationship of Microscopic Observations to Treatment

RICHARD L. TAW, *M.D.*, Los Angeles

• **Dysfunctional bleeding is not an entity, it is a symptom. With proper history, physical examination and laboratory aids a definitive diagnosis can be made. With this diagnosis rational and direct treatment may be instituted. Both diagnosis and treatment are outlined and discussed. When hormonal treatment is indicated, the type, amount and timing must be fitted to the patient's needs.**

THERE ARE SEVERAL DEFINITIONS of dysfunctional uterine bleeding but the one that is used in the clinic in which the author practices is: Bleeding from the uterine mucosa due to malfunction of the normal menstrual mechanism. This is preferred because it indicates a positive approach to the problem rather than one of exclusion. Since this definition includes difficulties that originate in the hypothalamus, pituitary, ovary and endometrium, it may be too inclusive for some readers, but there is some rationale for it from a therapeutic standpoint.

The ideas that are expressed here come mainly from a dysfunctional bleeding clinic that is operated as a division of the Gynecological Service of the Los Angeles County General Hospital. Patients are referred to this clinic from either the outpatient or inpatient services. Before reaching the clinic, each patient has a complete general history and physical examination as well as a gynecological history and pelvic examination, routine urinalysis, blood cell count and screening procedure for cancer of the cervix. In addition, each must have had a dilatation and curettage of the uterus including use of a polyp forcep. The protein-bound iodine determinations are ordered through our clinic, since this involves a separate study that is being conducted regarding the relationship of thyroid function to dysfunctional bleeding. The microscopic slides of pathological material for each patient visit are available in the clinic.

From the information obtained from the history, physical examination, laboratory and microscopic slides each patient is put into a category according to the classification shown in the adjoining column.

DISCUSSION

It has long been recognized that pituitary dysfunction is often the reason for menometrorrhagia. It may be the cause of any of the group listed under *Ovarian* in the foregoing classification. However, from a practical standpoint, this is ignored for two reasons: First, the bio-assay for gonadotropins is not sufficiently accurate except in gross abnormalities. Second, there are no products available to the clinician either to stimulate the pituitary or to adequately substitute with exogenous gonadotropins. Hence, cases in which we are certain bleeding is of pituitary origin are dealt with as if the ovary were at fault.

It is well established that anovulation is a cause of uterine bleeding, and endometrial hyperplasia is a familiar syndrome. However, hypoplasia also may be associated with this condition. Complete hypoplasia produces atrophy and amenorrhea but if (a) the amount of estrogen produced by the ovary is insufficient or (b) the ability of the endometrium to respond is reduced, hypoplasia will occur. The dividing line between hypoplasia and hyperplasia is not clear; one merges into the other, depending upon the amount of estrogen and the ability of the endometrium to respond. The microscopic features of gradual progression from hypoplasia to hyperplasia are shown in Figures 3, 4, 5, 6 and 7.

Classification of Cases of Dysfunctional Uterine Bleeding

I. Hormonal
- A. Pituitary
- B. Ovarian
  1. Anovulatory
     - (a) Hyperplasia
     - (b) Hypoplasia
  2. Ovulatory
     - (a) Corpus luteum irregularities
     - (b) Hyperplasia
     - (c) Hypoplasia

II. Endometrial
- A. Hyalinization
- B. No change.

Presented before the Section on Obstetrics and Gynecology at the 86th Annual Session of the California Medical Association, Los Angeles, April 28 to May 1, 1957.

From the Department of Gynecology, University of Southern California, and the Los Angeles County General Hospital, Los Angeles.

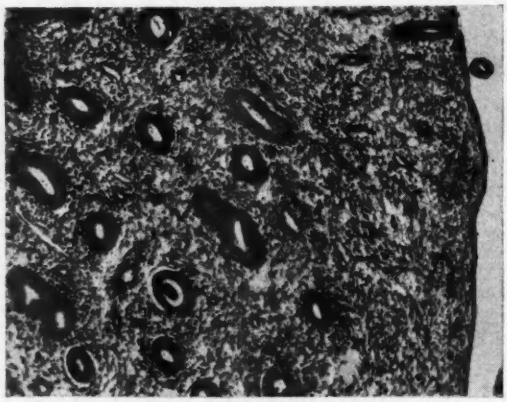

Figure 1.—Biopsy on seventh day of cycle, showing normal proliferative endometrium. Note uniformity of glands, stroma and blood vessels (×125).

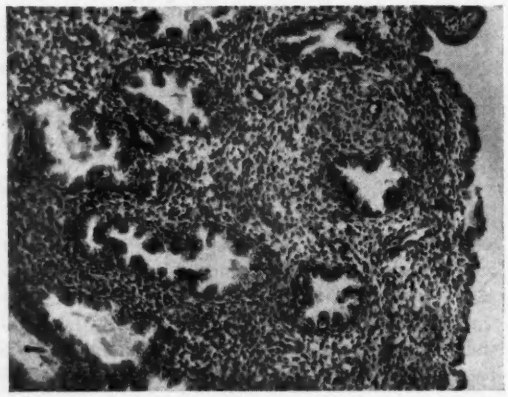

Figure 2.—Normal secretory endometrium, twenty-seventh day of cycle (×125).

Therapeutically, a woman who has anovulatory bleeding is not cured until she begins to ovulate, although the bleeding may be controlled by use of exogenous ovarian steroids. Cyclic therapy is usually used and there are several good methods. The object is to control the bleeding and to simulate a normal cycle. If the patient has had a cycle, it seems best to fit the artificial cycle to the patient's cycle. Assuming a 28-day cycle, our method is to give estrogen for 25 days and progesterone for the last 10 of the 25 days. Bleeding will usually start about the twenty-eighth day. We prefer stilbestrol because of factors of familiarity, cost, potency and wide variation in size of tablet available. We have not found a satisfactory progesterone product. The long-acting substances often produce a situation like irregular shedding, and the absorption from linguets is variable. The present practice is to use linguets if small amounts are needed and parenteral administration for large amounts.

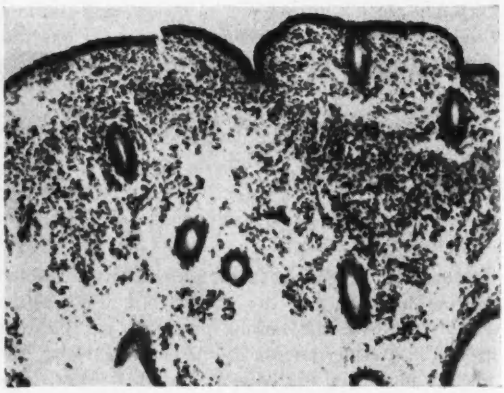

Figure 3.—Anovulatory hypoplasia, nearly atrophic endometrium. Patient had had bleeding for three weeks at time of dilatation and curettage (×125).

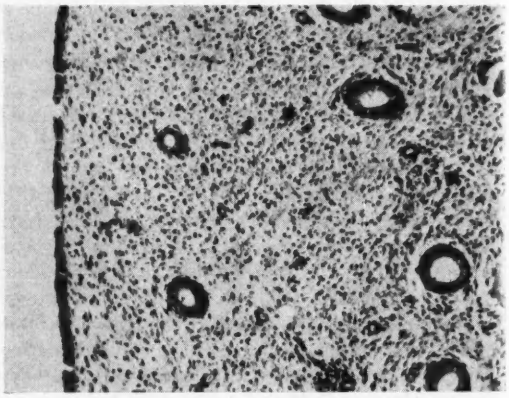

Figure 4.—Anovulatory hypoplasia. More response in stroma than in specimen shown in Figure 3, but little gland activity. Patient had had continuous bleeding for ten days at the time of curettage (×125).

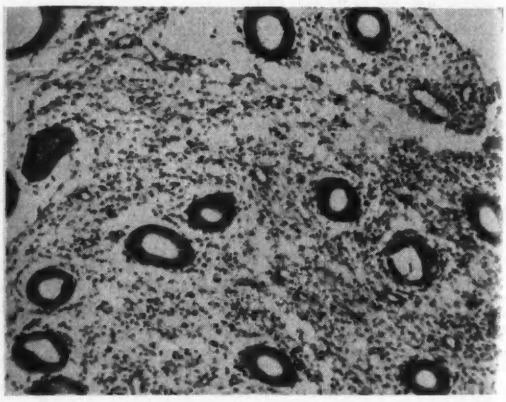

Figure 5.—Anovulatory hypoplasia. The stroma is thin but the cells lining the glands are tall and the glands are more numerous and larger than in Figure 4. Specimen was taken at time of dilatation and curettage on thirteenth day of bleeding (×125).

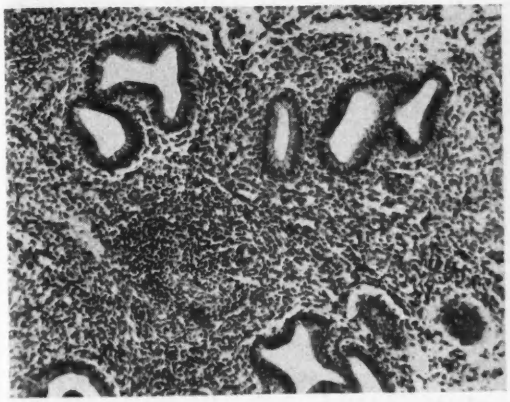

Figure 6.—Early anovulatory hyperplasia. Specimen taken at dilatation and curettage on seventh day of moderate bleeding. The stroma is dense, the glands active with variation in size and shape (×125).

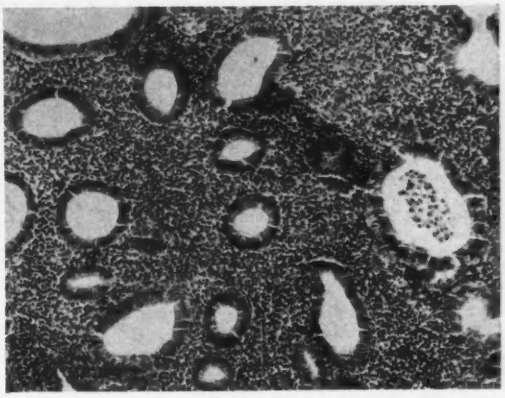

Figure 7.—Typical pattern of endometrial hyperplasia. Specimen taken at dilatation and curettage on twentieth day of bleeding (×125).

A patient with endometrial hyperplasia has too much estrogen as far as the endometrium is concerned. However, since estrogen is normally withdrawn, we give 1 to 3 mg. of stilbestrol daily for 25 days and 30 to 50 mg. of progesterone in the form of linguets from the fifteenth to the twenty-fifth day. This routine is repeated, starting on the second day of menses, for three cycles, the results being followed on basal temperature graphs. Use of hormones is then stopped to see what the effect will be without them. There is no limit to the number of times the process may be repeated. We have treated patients who had pregnancies after as much as six years of such a regimen.

As to dealing with endometrial hypoplasia, the amount of hormone given depends entirely upon the patient's need. Daily doses of 50 to 100 mg. of stilbestrol are not unusual and as much as 500 mg. has been used. Whatever the patient needs is given cyclically (just as for patients with hyperplasia) for two cycles and the amount given is then reduced each cycle until the minimum amount that will control the endometrium is reached. Progesterone is then added. We believe that in such cases the endometrium loses its ability to respond properly to estrogen but will regain it under regular, controlled cyclic stimulation. For instance, a patient who required 500 mg. of stilbestrol daily eventually responded better (as judged by endometrial biopsy) to 5 mg. daily. The progesterone response follows the same pattern, and that is the reason for withholding this hormone until responsiveness of the endometrium has been obtained. Hence, as in the use of desiccated thyroid, insulin or cortisone, the amount of ovarian steroid depends upon the patient response.

One important part of the treatment is continuous observation. When treatment is started, almost daily information is necessary.

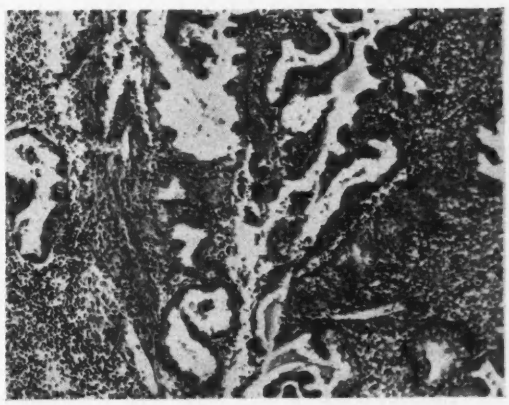

Figure 8.—Unshed secretory endometrium with irregular shedding. Specimen from curettage on fifth day of bleeding (×125).

That irregular shedding may cause menorrhagia has been well documented. In the normal menstrual mechanism, all the secretory endometrium is shed by the end of the third day of the period; hence the presence of any secretory endometrium beyond this time is, by definition, due to irregular shedding. For diagnosis, the dilatation and curettage is usually done on the fifth day (Figure 8). The curettage will usually take care of this condition. If it does not, we suppress the pituitary with stilbestrol for three cycles, using the basal temperature graph to prove suppression. The amount of stilbestrol necessary to do this will vary from patient to patient (usually it is between 3 and 15 mg. daily). Premature failure of the corpus luteum is manifest by early menses and is usually of no great importance.

True secretory hyperplasia is a rare condition.

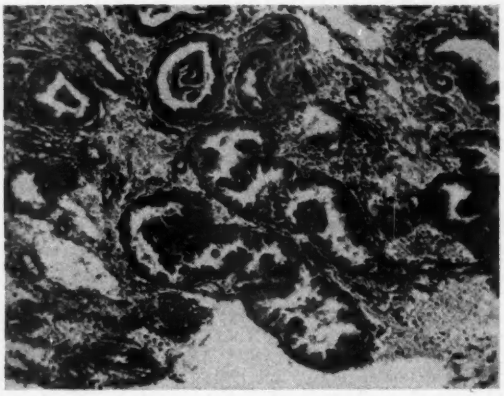

Figure 9.—Secretory hyperplasia. Specimen taken by curettage on twenty-sixth day of 28 to 30-day cycle for menorrhagia. When comparison is made with Figure 2, the lushness of the glandular response is evident (×125).

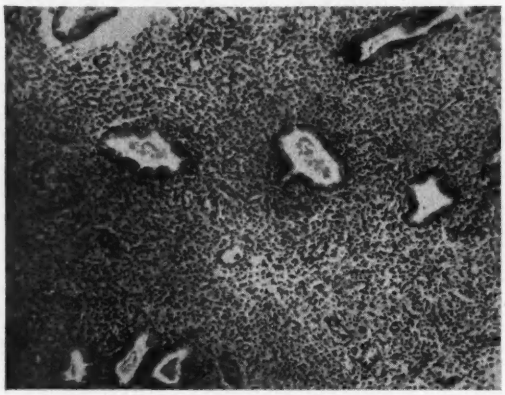

Figure 10.—Secretory hyperplasia. Dilatation and curettage was done on twenty-seventh day of 28-day cycle for prolonged menses (ten days). Note good stroma response but paucity and inactivity of glands (×125).

The patients may have premenstrual spotting and usually have menorrhagia. The endometrium is characterized by edema of the stroma and lush glandular response (Figure 9). This is the one condition in which testosterone is used for its ability to suppress the pituitary—usually a 10 mg. linguet daily, but more or less depending upon the patient response.

Although it is described as a cause of infertility, secretory hypoplasia is of interest in our clinic as a cause of bleeding. Figure 10 shows characteristic endometrial changes. The patients usually have prolonged menses with a tendency to bleed again at the time of ovulation. They respond well to daily (not cyclical) administration of small amounts of conjugated estrogens (0.3 to 0.675 mg.).

Hyalinization of the menstruating endometrium has been previously described as a cause of menorrhagia. Our interpretation of this difficulty is that it is a defect in the sloughing mechanism of the endometrium although it is often associated with irregular shedding. The microscopic findings are similar to those of the hyaline material occasionally associated with postpartum bleeding. However, in the specimen shown in Figure 11, menstruating endometrium, rather than decidua is present. Fortunately curettage ends the condition in most cases although it is likely to recur in six months to a year.

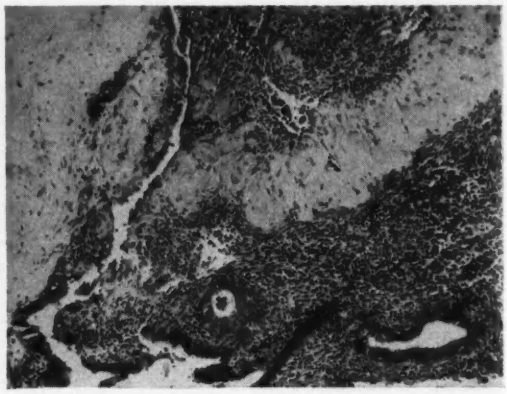

Figure 11.—Hyalinization of endometrium. Note masses of hyalin. Glands in this area are anovulatory. Dilatation and curettage was done on the fourteenth day of profuse bleeding that began on the twenty-ninth day of a normal 28 to 30-day cycle. The patient's last previous pregnancy was one year before the present irregularity (×125).

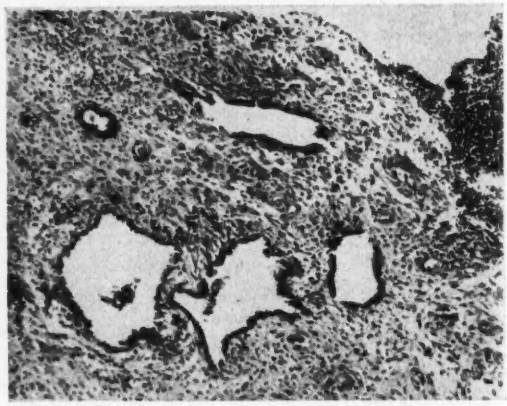

Figure 12.—Endometrial biopsy in case of target organ failure. Bleeding, in varying quantity, had been continuous for four months. Repeated attempts to control with estrogen or progesterone had failed. At the time this specimen was obtained, the patient had been receiving 50 mg. of stilbestrol daily for 20 days and 125 mg. of Delalutin® progesterone every two days for ten days, and bleeding was unabated (×125).

Finally, there are rare cases in which the endometrium has lost the ability to respond properly to the ovarian steroids (Figure 12). All such cases

TABLE 1.—*Results of Treatment in 119 Cases of Dysfunctional Uterine Bleeding*

Classification	No. Cases	Results		
		Good	Poor	Failure
Ovarian	112			
Anovulatory	78			
Hyperplasia	8	7	1	----
Hypoplasia	70	60	8	2
Ovulatory	34			
Corpus luteum irregularity	29	21	4	4
Hyperplasia	2	2	----	----
Hypoplasia	3	3	----	----
Endometrial	7			
Hyalinization	4	2	2	----
End organ failure	3	----	----	3
Results, all cases		95	15	9

observed by the author were associated with anovulation and the patients were near menopausal age. Care must be taken to differentiate cases of this kind from anovulatory hypoplasia, for in the latter condition the endometrium will regain the ability to respond. Lack of response must be proved by repeated endometrial biopsies following adequate exposure to ovarian hormones. The only satisfactory treatment is removal of the uterus or destruction of the endometrium by irradiation.

RESULTS

The results obtained by the use of the foregoing diagnostic attitudes and methods of treatment in 119 patients observed in the clinic in the period 1951-56 and on whom there was adequate follow-up data, are given in Table 1. The results were considered good if the patient had normal ovulatory cycles for at least six months or she became pregnant; poor if she was still under treatment. If the uterus was removed the result was deemed failure.

COMMENTS

To compare the results here reported with results obtained in any but the same kind of clinic treating the same kind of patients would be inequitable. The patients observed at the dysfunctional bleeding clinic at the Los Angeles County General Hospital usually come to the clinic only because they are sick, and it is extremely difficult to get a patient who has recovered to report that she is well. Another factor is that many patients with dysfunctional bleeding go through the inpatient or outpatient service of the hospital, recover because of time or curettage, and do not reach the clinic. This tends to make the clinical material proportionally high in "problem cases." Another peculiarity affecting the data is that many of the patients are kept under observation much longer than they would be in private practice, owing to the special interest of the clinic's medical personnel. The distribution of diagnoses also is peculiar to the kind of patients, there being a relatively higher incidence of anovulatory hypoplasias and lower incidence of irregular shedding than might occur in patients dealt with in another stratum of practice.

Emphasis should be placed upon the fact that dysfunctional bleeding is not an entity but a symptom. The approach to it should be the same as that to any problem in medicine. A history is taken, physical examination done and laboratory and diagnostic procedures carried out. With the data obtained by these means, definitive diagnosis is made and the patient treated accordingly. This adherence to sound medical principles is emphasized because of the author's belief that often in difficult cases failure can be laid to lack of systematic and logical approach to the problem.

The endometrial response to therapy—the duration and intervals between bleeding and the microscopic observation of changes in endometrial material removed for biopsy—are the best guides as to how much and how intensely to treat.

3741 Stocker Street, Los Angeles 8.

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Discussion by J. G. MOORE, *M.D., Los Angeles*

Dr. Taw has presented a concise analysis of a series of patients who present a "malfunction of the normal menstrual mechanism." His definition of functional uterine bleeding would presume that we know the mechanism of normal menstruation. Such is not exactly the case, as is indicated by several reported series of women who have normal ovarian cycles and histologically normal endometrial cycles in the absence of visible menstrual flow. However, the positive approach of designating a specific malfunction in each case, even though it cannot always be proven, is appealing and lends itself well to the selection of therapy.

Dr. Taw's series is somewhat unique in that the patients had bleeding problems sufficient to force them to endure the rigors of a county hospital outpatient clinic. It represents a selection from a great number of inpatients who had dilatation and curettage for abnormal uterine bleeding. His patients are well studied from the standpoint of general physical condition, nutritional status, thyroid function and repeated endometrial biopsy. Perhaps as important as any factor is the review of histologic sections with the patient each time she attends the clinic. The frequent review of such sections, while outlining the regimen of management for any given patient, tends to focus treatment.

The review of Dr. Taw's histologic sections bears out that abnormal bleeding may result from endometrium of any type. Certainly the specimens show beautiful gradations between pronounced hypoplasia and decided hyperplasia. I am sure that Dr. Taw would be the first to state that the functional ability of the endometrium is not always associated with the degree of hypoplasia or hyperplasia of a given type of endometrium. It would be nice to have sections of proliferative endometrium from a series of normally menstruating women to show that the various degrees of hypoplasia and hyperplasia are not equally common in control groups.

I am impressed that Dr. Taw has kept his classification simple. He eliminates questionable deficiencies as well as subclinical aberrations of the blood coagulation mechanism. He has thus eliminated many of the impericisms of treatment such as hesperidin, cortisone and toluidine blue which have been so illogically employed in the management of functional uterine bleeding. This simplification results in practically all patients being managed with cyclic ovarian steroids for such periods of time as will allow the normal pituitary ovarian cyclicity or normal endometrial response to be reestablished. This concept is in keeping with the experience that functional uterine bleeding is largely a self-limiting condition and once organic disease has been ruled out with a curettage, most patients will in time resume a normal menstrual pattern.

I am largely in agreement with Dr. Taw concerning many of the finer points of management. The polyp forceps is certainly essential to the proper method of effecting a dilatation and curettage. Stilbestrol is a logical estrogen to use in instituting cyclic steroid therapy and the more expensive conjugated estrogens are not necessary with the great majority of patients. On the other hand, I have never been satisfied with linguets as a method of administering progesterone, for in a considerable percentage of patients I have been unable to obtain a progestational effect on the endometrium of anovulatory patients. I have had much better results with a single dose of 25 mg. (1 cc.) aqueous suspension progesterone given intramuscularly. Recently, we have effectively used 10 mg. tablets of 17-ethinyl-19-nortestosterone on each of four days before the expected onset of flow. This latter preparation has been most effective in producing a progestational effect on the endometrium and works well when added to stilbestrol during the third week of cyclic steroid therapy.

No. 1 Killer

Heart disease and cancer claim more lives than automobile crashes but lay their heaviest toll on those in later life. The automobile, when it kills, takes more *years* of life.

Reiter Protein Complement Fixation Test

A Preliminary Comparison of the TPI Test with the Complement Fixation Test Employing a Soluble Protein Antigen Derived from the Reiter Strain

JAMES N. MILLER, *Ph.D.*, RUTH A. BOAK, *M.D.*, and CHARLES M. CARPENTER, *M.D.*, Los Angeles

• **A comparative study of the specificity of the Reiter protein complement fixation (RPCF) test and the Treponema pallidum immobilization (TPI) test on 180 sera showed that the results in 178 instances or 98.9 per cent were in agreement.**

The sensitivity of the RPCF test, when compared to the TPI test, on 189 sera from patients known to have syphilis was in agreement in 182 or 96.3 per cent, *assuming* a correlation exists between positive TPI and both the "reactive" or "weakly reactive" RPCF test results.

As to reproducibility of results, the RPCF test results agreed in 84 of the 87 sera tested (95.4 per cent). The sera were tested at least three times on different days.

Anticomplementary reactions were observed in three of 91 normal sera.

ALTHOUGH THE Treponema pallidum immobilization (TPI) test, developed by Nelson and Mayer,[17] is at present accepted to be the most dependable test for the diagnosis of syphilis, the laborious techniques involved limit its use. As a result, several investigators have been searching for tests comparable in sensitivity and specificity for routine use in public health laboratories. Within the past few years, attention has been focused on the Treponema pallidum agglutination (TPA), Treponema pallidum immune adherence (TPIA), and the Treponema pallidum complement fixation (TPCF) tests. The advantages and disadvantages of these procedures have already been reported.[3,7,9,10,12,14,15,18,19,20,21]

In 1950, D'Alessandro, Oddo and Dardanoni[5] observed the avirulent Reiter strain of T. pallidum to contain four antigens, (1) a treponemal specific protein fraction, (2) a reactive lipoidal fraction identical with tissue lipoidal antigen, (3) a nonreactive polysaccharide, and (4) a nonreactive "organ" specific antigen. D'Alessandro and Dardanoni[6] further observed that the soluble antigen prepared from the protein fraction reacted with antisyphilitic sera in the complement fixation test. The antigen did not react with sera from animals "immunized" with a lipoidal antigen-foreign protein mixture. On the other hand, the lipoidal fraction gave weakly positive reactions in tests with sera from the "immunized" animals.

The use of a phenolized saline antigen comprising the whole cell Reiter spirochete has given results comparable to the sensitivity and specificity of the standard serologic tests (STS). A small percentage of sera from patients considered to be biologic false positive reactors and tested with the Reiter antigen showed reactivity, however.[22] Similar results have been reported in studies comparing the TPI test with the complement fixation test using the whole cell Reiter spirochetes as antigen.[8,11,16,24] Presumably, such results are due to the presence of lipoidal material in the spirochete. With the development of a soluble purified protein antigen, preliminary studies were undertaken to compare results obtained in the Reiter protein complement fixation (RPCF) test with those obtained in the TPI test.

From the Department of Infectious Diseases, School of Medicine, University of California, Los Angeles 24.

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Submitted October 21, 1957.

MATERIALS AND METHODS

The soluble protein antigen used in the Reiter complement fixation test was prepared in a lyophilized state by Dr. J. H. De Bruijn of the National Institute of Public Health, Utrecht, Netherlands, according to the method of D'Alessandro and Dardanoni[6] and was supplied by Dr. Charles R. Rein. The antigen was reconstituted, as directed, with an equal volume of sterile distilled water and stored at 4° C. Immediately before use, the reconstituted antigen was diluted 1:80 with sterile 0.85 per cent salt solution and employed in a modified one-fifth volume Kolmer technique according to the TPCF test described by Portnoy and Magnuson.[19] The results of the test were interpreted as follows: 3+ and 4+, reactive; ± to 2+, weakly reactive; negative, nonreactive.

The TPI test was carried out according to the method of Nelson and Mayer[17] with modifications as described by Magnuson and Thompson,[13] Thompson and Magnuson,[23] and Boak and Miller.[1]

TABLE 1.—*Comparison of Specificity of the TPI and RPCF Tests*

Classification	Total Sera	TPI Negative: RPCF Nonreactive	TPI Negative: RPCF Weakly Reactive	TPI Negative: RPCF Reactive	Anticomplementary	Per Cent Correlation
No history of syphilis, nonreactive STS*	88	88	0	0	3	100.0
No history of syphilis, reactive STS*	92	90	0	2	0	97.8
Total	180	178	0	2	3	98.9

*VDRL and Cardiolipin Kolmer tests.
Abbreviations: TPI = Treponema pallidum immobilization. CF = Complement fixation. RPCF = Reiter protein complement fixation. STS = Serologic test for syphilis. VDRL = Venereal Disease Research Laboratory (Chamblee, Georgia).

TABLE 2.—*Comparison of Sensitivity of the TPI and RPCF Tests*

Classification (Treated Cases)	Total	TPI Positive: RPCF Reactive	TPI Positive: RPCF Weakly Reactive	TPI Positive: RPCF Nonreactive	TPI Negative: RPCF Reactive	TPI Negative: RPCF Weakly Reactive	TPI Negative: RPCF Nonreactive	Correlation of RPCF and TPI Totals
No history syphilis, reactive STS*	115	110	5	0	0	0	0	115/115
No history syphilis, nonreactive STS*	11	10	1	0	0	0	0	11/11
Early syphilis, reactive STS	38	26	3	1	1	2	5	34/38
Early syphilis, nonreactive STS	9	5	1	0	1	1	1	7/9
Late syphilis, reactive STS	7	5	1	0	0	0	1	7/7
Late syphilis, nonreactive STS	1	1	0	0	0	0	0	1/1
Congenital syphilis, reactive STS	5	4	1	0	0	0	0	5/5
Congenital syphilis, nonreactive STS	3	2	0	1	0	0	0	2/3
Total	189	163	12	2	2	3	7	182/189

*VDRL and Cardiolipin Kolmer tests.
Abbreviations: TPI = Treponema pallidum immobilization. STS = Serologic test for syphilis. RPCF = Reiter protein complement fixation. VDRL = Venereal Disease Research Laboratory.

EXPERIMENTAL RESULTS

The Specificity of the RPCF Test

RPCF tests were carried out on 91 sera from persons with no history of syphilis, nonreactive STS, and with a negative TPI test. Three sera were anticomplementary. All of the remaining sera showed nonreactive RPCF tests (Table 1). Quantitative titrations could not be carried out on the three anticomplementary sera because of lack of sera. Ninety or 97.8 per cent of 92 sera from patients with no history of syphilis, a reactive STS, and a negative TPI test showed nonreactive RPCF tests. Thus, 178 or 98.9 per cent of 180 sera on which valid results were obtained showed nonreactive RPCF tests, indicating the high specificity of the antigen.

The Sensitivity of the RPCF Test

The sensitivity of the RPCF test was determined by testing 189 sera from treated patients known to have or to have had syphilis, on the basis of a positive TPI test or darkfield positive lesions. Too few samples of serum were tested to compare the results of the two tests in the different stages of the disease. Assuming that correlation exists between positive TPI test results and both reactive and weakly reactive RPCF results, the two procedures correlated in 182 or 96.3 per cent of the 189 sera tested (Table 2).

The Reproducibility of the RPCF Test Results

The reproducibility of the RPCF test results was observed on 87 sera tested at least three times on different days. Fifty-six sera were from patients with no history of syphilis, reactive STS, and a negative RPCF test result. Eight were from patients with a history of syphilis and a negative RPCF test result, and the remaining 23 were from patients with a history of syphilis and a reactive or weakly reactive RPCF test result. The results of the tests on 83 or 95.4 per cent of the 87 sera were in agreement and those obtained on sera from four patients with a history of syphilis did not agree.

DISCUSSION

The comparative studies on the TPI and RPCF tests presented in this preliminary report indicate a satisfactory degree of sensitivity and specificity for the RPCF test employing a purified protein antigen from the Reiter avirulent strain of T. pallidum. The data are in accord with the recent report of Cannefax and Garson,[4] who observed that the results of the RPCF test compared favorably with those obtained with the TPI and TPCF tests. In the former procedure, the antigen was prepared similarly to that used in the present study.

A disadvantage of the RPCF test which often occurs in complement fixation procedures is the anticomplementary reaction. In this study, three such reactions were observed in the presence of normal sera, but no anticomplementary results were observed with the TPI test on the same sera. The percentage of anticomplementary reactions obtained with the RPCF procedure when testing larger numbers of samples is under investigation.

The significance of the "weakly positive" RPCF reaction in the presence of a positive TPI test is difficult to evaluate at present. Although the "weakly positive" reactions were included in the correlation of the two tests, obviously a weakly positive result reflects a lower degree of sensitivity than a test resulting in a positive reaction. On the other hand, five patients with confirmed history of syphilis and negative TPI test results showed some degree of reactivity in the RPCF test. The preliminary study suggested that, in the presence of a 98.9 per cent specificity, any reactivity in the RPCF test presumably indicates infection with virulent T. pallidum. Further studies with a larger number of selected sera are in progress to formulate a dependable interpretation of the reactions.

The satisfactory reproducibility of the RPCF test results compares favorably with the reproducibility of the TPI test results obtained by Boak, Miller and Carpenter.[2] This, together with the high degree of sensitivity and specificity of the test, indicates that the RPCF test may become a dependable adjunct to the battery of standard tests for syphilis.

University of California at Los Angeles School of Medicine, Los Angeles 24 (Carpenter).

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Treponemal Serologic Tests

Experiences of the Bacteriology Laboratory, California State Department of Public Health

ALCOR S. BROWNE, *Ph.D.*, and EDITH COFFEY, *B.A.*, Berkeley

• **In a study of the relationship of clinical impression regarding syphilis and age, sex and pregnancy status to treponemal serologic test reactivity, it was noted that in diagnostic "problem cases" the standard lipid serologic test titers did not differentiate between syphilitic and biologic false positive reactors. Preliminary data indicated that heroin addiction may be a source of biologic false reactions and that pregnant women with standard serologic test reactivity have a lower treponemal reactivity rate than other women with lipid serologic reactivity.**

NOTWITHSTANDING the general downward trend in reported cases of syphilis during the past decade, this infection represents a continuing problem to clinicians, epidemiologists and microbiologists.

An ever present problem to clinicians and laboratorians is the biologic false positive (BFP) reaction with the standard lipid tests for syphilis in patients in whom there is no historical, clinical or epidemiological evidence of syphilitic infection. Moore and Mohr[6] expressed the belief that in certain population groups at least half the persons with serologic reaction in mass blood-testing programs do not have syphilis. Although these reactors represent a small fraction of the total number of persons tested in such a program, they present a very real problem to physicians.

Following the description of the Treponema pallidum immobilization (TPI) test in 1949 by Nelson and Mayer,[7] serologic procedures employing treponemal antigens have become available which are considered to possess a high level of sensitivity and specificity in the treponematoses. In a collation of results of the clinical significance of the TPI on some 10,035 sera and 323 specimens of spinal fluid, Nielsen and Reyn[8] reported that the general sensitivity of the TPI test appears to be high except in early syphilis; the TPI result was positive in about 60 per cent of the cases of primary syphilis studied, in about 90 per cent of the secondary cases and in nearly 100 per cent of the cases of longer duration. These investigators also reported a high level of specificity.

Although his study series was smaller, Zellerman[10] noted false treponemal test results in only 0.3 per cent of the cases studied.

The Treponema pallidum complement fixation test (TPCF) described by Portnoy[9] in 1955 is reported to be more sensitive in early syphilis than is the TPI test; and the false-positive incidence is reported to be less than 1 per cent.[4]

The treponemal testing program of the United States Public Health Service has provided a much needed opportunity for an evaluation of the reactivity patterns of some of the standard serologic tests for syphilis in diagnostic problem cases. It has been repeatedly shown that the standard serologic tests for syphilis demonstrate satisfactory sensitivity in cases of syphilis and a high level of specificity in selected nonsyphilitic persons. However, little has been published concerning the reactivity level of these tests in diagnostic problem cases. Indeed, until the advent of the treponemal tests, it was extremely difficult to establish a standard of reference whereby the serologic tests employing lipid antigens could be evaluated.

Data presented in this paper concern the relationship of treponemal tests and the reactivity level of standard serologic tests employing lipid antigens. These tests were performed respectively in the Venereal Disease Research Laboratory (VDRL) at Chamblee, Georgia, and the California State Division of Laboratories. The term *lipid test* is used to describe standard serologic tests employing either crude lipoidal or cardiolipin-lecithin antigens. The serologic tests selected were the VDRL slide test and the Kolmer complement fixation test. Both of these tests employ cardiolipin-lecithin antigens. The standard Kolmer test employs an antigen in which the ratio of lecithin to cardiolipin is 1.66 to 1. In addition to this antigen, the Kolmer test was also performed with two less sensitive antigens. One of these was the crude lipoidal antigen known as "New Improved Kolmer Antigen,"[5] which is still used in a number of laboratories, and the other was a cardiolipin-lecithin antigen with a ratio of lecithin to cardiolipin

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Dr. Browne is Chief, Bacteriology Laboratory of the California State Department of Public Health, and Miss Coffey is an Assistant Microbiologist in the Serology Section of the same laboratory.

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TABLE 1.—*Clinical Impression and Treponemal Reactivity on 1,290 Specimens Submitted for TPI Testing*

Clinical Impression	Number	Per Cent	TPI Reactivity			
			Number		Per Cent	
			Reactive	Nonreactive	Reactive	Nonreactive
Syphilis	224	17	156	68	70	30
BFP	941	73	415	526	44	56
Not stated	125	10	67	58	54	46
Total	1,290	100	638	652	49	51

Abbreviations: TPI = Treponema pallidum immobilization; BFP = Biologic false positive.

TABLE 2.—*TPI Reactivity of 1,286 Patients by Age and Sex*

Age Group—Years	Males			Females		
	Total No.	TPI Reactive		Total No.	TPI Reactive	
		No.	Per Cent		No.	Per Cent
<16	10	4	40	6	0	0
16 to 45	316	152	48	558	238	43
46>	192	116	60	204	128	63
All ages	518	272	53	768	366	47

TPI = Treponema pallidum immobilization.

TABLE 3.—*TPI Reactivity in 768 Women According to Pregnancy Status*

Pregnancy Status	Total No.	TPI Reactive		TPI Nonreactive	
		No.	Per Cent	No.	Per Cent
Pregnant	135	38	28	97	72
Pregnancy not indicated	633	328	52	305	48

TPI = Treponema pallidum immobilization.

of over 11 to 1 and a sensitivity about equal to the new improved Kolmer antigen. This formulation of Allen and Mason[2] is now used in the National Health Department Laboratories in Canada. However, in this study it has been used only on an experimental basis and individual test results have not been reported to physicians.

The USPHS Venereal Disease Research Laboratory through State and Territorial Health Departments has offered a nationwide treponemal testing service since January 1955. The criteria established by the USPHS required that specimens be submitted only on diagnostic problem cases in which there was a possible discrepancy between clinical opinion and serologic test results. All patients with reaction to lipid tests, except pregnant women, were to be followed with these tests for a minimum of three months before specimens were sent for treponemal testing. Physicians were further required to submit a clinical data sheet for each patient. The information requested included: History of syphilis in the patient or his family, evidence of other treponemal or other venereal disease, evidence of certain diseases thought to cause biologic false positive reactions in the standard tests, record of previous standard test results, the physician's clinical impression of the significance of these results—that is, whether he thought them due to biologic false reactivity or to syphilis. No data were requested regarding pregnancy or drug addiction. Requirements were established regarding collection and submission of specimens in an effort to insure reliability of test results.

In California whole blood specimens accompanied by the clinical data sheet and a syphilis serologic test request form were submitted to the State Division of Laboratories by private physicians, local health departments and venereal disease clinics. A portion of serum accompanied by the clinical data sheet was sent to the Venereal Disease Research Laboratory for treponemal testing. When there was an adequate amount of serum, a portion was reserved for testing in the California State Laboratory with the standard lipid tests. The procedures employed in performing these tests are outlined in the 1955 Manual of Serologic Tests for Syphilis.[1] Data from the history sheet, correspondence and the state serology form as well as standard and treponemal test results were entered on marginal punch cards. This procedure afforded an opportunity for comparison of lipid and treponemal test reactivity on "problem" sera in California.

From January 1955 to January 1957, 1,290 sera were tested in the Venereal Disease Research Laboratory by the TPI and in the California State Laboratory with the lipid tests indicated. Because of serum limitations, all four standard serologic tests were not

TABLE 4.—*Agreement of Individual Lipid Tests with Treponemal Test*

STS Test*	Number Sera Tested	Per Cent Agreement of STS with Treponemal Test: Treponemal Reactive Sera	Treponemal Nonreactive Sera	Overall Agreement with Treponemal Test
VDRL slide	1,576	93	42	68
Kolmer's cardiolipin (1)	1,530	86	46	66
Kolmer lipoidal (5)	1,320	55	80	68
Kolmer Canadian (2)	347	59	83	73

*Numbers in parentheses indicate reference citation.
Abbreviations: STS = Standard serologic test; VDRL = Venereal Disease Research Laboratory test.

performed on every specimen. Early in 1957, the testing procedure at the Venereal Disease Research Laboratory was changed from the TPI to the Treponema pallidum complement fixation (TPCF) test. From January through March 1957, 290 additional sera were tested in the two laboratories. The comparison of STS reactivity with treponemal test reactivity was essentially the same for the TPI and the TPCF. Therefore, in many instances in this paper, no distinction will be made as to which treponemal test was performed. For purposes of comparison and simplification, weakly reactive and reactive qualitative test results are grouped as reactive in both the standard and treponemal tests.

Treponemal Reactivity by Clinical Impression (Table 1)

A physician submitting a specimen was asked to state if in his opinion the serologic test for syphilis (STS) reactivity represented syphilis or a biologic false positive (BFP) reaction. A clinical impression of syphilis was indicated for 17 per cent of the patients, an impression of BFP for 73 per cent, and no impression was stated for 10 per cent. Of the 1,290 specimens submitted for TPI testing, 49 per cent were TPI test reactors and 51 per cent were TPI nonreactors. The TPI test showed reaction in 70 per cent of the patients with a physician's impression of syphilis, in 44 per cent of the patients believed by the physician to have BFP, and in 54 per cent of the patients about whom no impression was given.

Treponemal Reactivity by Age, Sex, and Pregnancy Status (Tables 2 and 3)

There were 1,286 specimens submitted for TPI testing upon which data were given regarding the patient's sex and age. Five hundred and eighteen or 40 per cent of these specimens were from males and 768 from females. The number of specimens in the age group under 16 years was considered too small to permit meaningful analysis regarding TPI reactivity in this group. In the age group of 46 years and over, 60 per cent of men and 63 per cent of women had TPI reactivity. In the 16-45 year group, 48 per cent of males and 43 per cent of women were reactive.

Although the history form did not ask for a statement of pregnancy status, the physicians submitting the specimens noted pregnancy in 135 women, all of whom were in the 16 to 45 age group. Data for TPI reactivity according to pregnancy status are given in Table 3. Of the 135 women known to be pregnant, only 38 (28 per cent) were TPI reactive. In all other women, TPI reactivity was 52 per cent, which closely approximates the 53 per cent treponemal reactivity of all males.

Treponemal Reactivity in Other Conditions

Because of a lack of consistency in the data submitted on the history form employed in this study, an evaluation of treponemal test reactivity in conditions commonly thought to cause false positive STS results was not made. However, it is of interest that 25 heroin addicts who were presumably nonsyphilitic but had standard test reaction, had only half the incidence of treponemal reactivity observed with other patients.

Comparison of STS and Treponemal Reactivity (Table 4)

In this group of sera from problem patients, the VDRL slide test results agreed best with the treponemal reactive results and poorest with the treponemal nonreactivity. Of 1,576 sera tested by the VDRL, 93 per cent were reactive with the treponemal reactive sera but only 42 per cent were nonreactive in the treponemal nonreactive sera. The cardiolipin Kolmer test was the next most reactive test. In results on 1,530 sera tested, 86 per cent agreed with the treponemal reactors and 46 per cent agreed with the treponemal nonreactors. In 1,320 sera, the lipoidal Kolmer test was reactive in only 55 per cent of the treponemal reactive specimens but was nonreactive in 80 per cent of the treponemal nonreactive sera. Testing procedures were not started with the Canadian cardiolipin Kolmer antigen until November 1956. From that date to May of 1957, 347 sera were tested. The Canadian Kolmer test was reactive in 59 per cent of the treponemal reactors tested and was nonreactive in 83 per cent of the treponemal nonreactive sera, which closely approximates the reactivity agreement of the lipoidal Kolmer test.

Overall agreement between the treponemal tests and each of these lipid tests was between 66 and 73 per cent.

Whenever possible, several STS were performed on each specimen submitted for treponemal testing to determine if a battery of tests would be helpful in solving these serologic problems. There were 1,302 specimens upon which it was possible to perform the VDRL slide test and the Kolmer test with cardiolipin and lipoidal antigen (Table 5). In 78 per cent of the sera that were reactive to all three STS, the TPI was also reactive. The incidence of TPI reactivity dropped to 50 per cent on sera reactive to only two STS, and to 33 per cent on sera reactive to only one STS. In 89 per cent of the sera where all three STS were nonreactive, the TPI was also nonreactive.

TABLE 5.—*Lipid and Treponemal Test Reactivity on 1,302 Specimens*

STS*	Total Specimens	Treponemal Test: Reactive No.	Reactive Per Cent	Nonreactive No.	Nonreactive Per Cent
Reactive in 3 STS	426	330	78	96	22
Reactive in 2 STS Nonreactive in 1 STS	400	198	50	202	50
Reactive in 1 STS Nonreactive in 2 STS	252	83	33	169	67
Nonreactive in 3 STS	224	25	11	199	89

*Tests employed: Venereal Disease Research Laboratory slide; Kolmer with cardiolipin and lipoidal antigens.

Relationship Between STS Titer and Treponemal Reactivity

If the available specimen was large enough, quantitative tests were performed in an effort to determine the relationship of STS titer to treponemal reactivity on sera from patients presenting diagnostic problems. In sera reactive in the VDRL slide test (Chart 1), there was no difference in titer between presumably syphilitic sera (TPI reactors) and presumably biologic false positive sera (TPI nonreactors). Ninety per cent of the reactions occurred at dilutions lower than 1:8. Although not shown in the chart, the distribution of titers obtained in the Kolmer test with lipoidal and with Canadian antigen very closely paralleled that obtained in the VDRL slide test. The charted curve of the standard cardiolipin Kolmer antigen test results was similar to that of the VDRL, but it was reactive at a somewhat higher titer, some 40 per cent of the sera showing reaction in dilutions of 1:8 or higher.

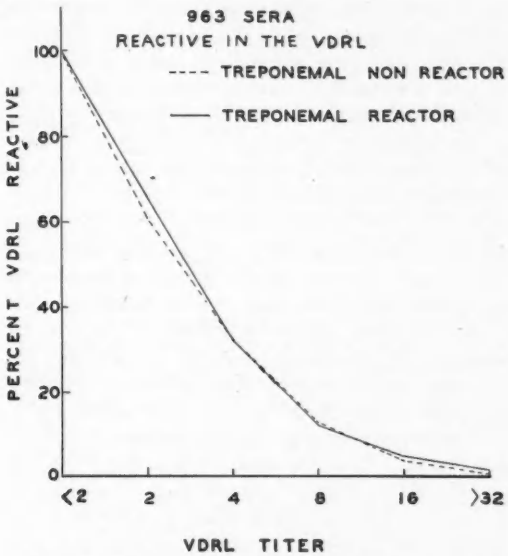

Chart 1.—Showing lack of agreement between VDRL test (Venereal Disease Research Laboratory) and treponemal immobilization test.

DISCUSSION

The correlation between clinical opinion and treponemal reactivity reported here is similar to that previously reported by Bossak and associates[3] for the United States as a whole. In over 50 per cent of the cases in which the physician considered the STS reaction a false positive one, the TPI bore out the clinical impression. However, over 40 per cent of the presumably false reacting patients were treponemal reactive.

The data presented in Chart 1 clearly indicate that in the individual patient it is impossible to predict treponemal reactivity from standard serologic test reactivity. In patients presenting diagnostic problems, there was no correlation between treponemal reactivity and the amount of reagin present as determined by quantitative STS. In this series of tests, several specimens with STS titers reaching 1:5,000 were treponemal nonreactive. However, when a battery of STS was performed, the greater the number of reactive lipid tests, the greater the chance that the treponemal test would also be reactive. Conversely, the greater the number of nonreactive lipid tests, the greater the chance that the treponemal test would also be nonreactive. While statistical data cannot apply to an individual patient, the finding of lipid reactivity in two or more STS set at different levels of reactivity may offer a clue for the deeper probing into the medical, physical and social history of patients who have such reactivity. It would seem equally important to do further studies of a patient with discrepancy between results of serologic tests. An appreciable number of patients showing serologic

reactivity over a period of three months or more in only one or two of several STS, were reactive to the treponemal tests. Thus, it would appear that any presumably false serologic reaction which cannot be definitely attributed to some other condition and which persists for a period of at least three months should be checked by one or more of the available treponemal procedures.

The finding of a significantly lower level of TPI reactivity in pregnant women than in all other women tested is of interest. However, it must be pointed out that a different basis of selection was employed for the two groups. Pregnant women were not required to be followed for three months with the standard tests as were all other patients. It is probable that some of the treponemal nonreactors in the pregnant group would not have been included in the study had these women been followed for three months with the lipid tests as were other patients in this study. Nonetheless, there is evidence that pregnancy is of itself a cause of biologic false reaction of the acute type. It is hoped that studies now in progress will provide additional information on both pregnancy and heroin addiction as possible causes of false positive reactions in the standard tests.

Although the VDRL test results gave the poorest agreement with treponemal test nonreactors in this series of problem specimens it should not be inferred that this test is unsatisfactory for routine use. Experience is quite to the contrary. Routine serologic tests are not specific for syphilis but react in nearly 100 per cent of late primary, secondary and early latent cases. In determining test reactivity levels, serologists reporting on studies must achieve a nice balance between ability to react in cases of luetic infection and inability to react in serum from presumably nonsyphilitic individuals. It has been a general experience that as test sensitivity increases, specificity decreases. Regardless of the sensitivity level, serologic tests for syphilis must be subject to control of reproducibility of test results at the operating level and not be too cumbersome to perform. Of tests in common use, the VDRL seems best to meet the needs of clinicians and of laboratories in these respects.

Perhaps a word is needed about the validity of data involving the smaller number of tests employing the Canadian antigen formulation in the Kolmer test. When other STS antigens were evaluated in terms of TPI results at the same stage of experience, there was no decided deviation from that herein reported. We feel the data given are a reliable index of future experience.

In the present series of patients, there was no known bias in selection according to racial or socioeconomic status. The patients would appear to represent a cross-section of the population of California. However, data are needed to evaluate the influence of these factors in determining treponemal reactivity.

2151 Berkeley Way, Berkeley 4 (Browne).

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Splenectomy in Blood Dyscrasia

MORTON M. WOOLLEY, *M.D.*, Los Angeles, and
EUGENE J. JOERGENSON, *M.D.*, Glendale

• **The decision for splenectomy must be based on a knowledge of the three functions of the spleen: Hematopoiesis (usually ceasing during fetal life but sometimes resuming when bone marrow function fails); filtration of abnormal and senescent cells and control of bone marrow activity, most probably humoral.**

When bone marrow function fails, splenectomy is contraindicated since splenic hematopoiesis becomes a vital function. On the other hand, when a large proportion of erythrocytes are abnormally shaped (spherocytes), although otherwise adequate, the spleen may trap these cells in its filter and destroy large numbers. Splenectomy is beneficial in almost every case of congenital spherocytosis, but in only half the cases of the acquired defect.

In panhematocytopenia, thrombocytopenia and neutropenia, all apparently due to depression of hematopoiesis by endocrine or other action of the spleen, splenectomy may be beneficial if medical therapy fails.

A surgeon undertaking splenectomy should recognize two special problems: (1) The presence of accessory spleens, which if not removed may negate the effects of the operation, and (2) the apparently high rate of infection in infants and children who have undergone splenectomy.

"THE SURGEON is often placed in a somewhat delicate position when asked to see a patient about splenectomy, unless the indications are clear and well-established, as in familial hemolytic anemia. By the time the surgeon's opinion is asked, the physician, in collusion with the hematologist, has already probably decided the issue. The surgeon may thus find himself relegated to the humble position of the craftsman, for he cannot hope to master the intricacies of hematology to an extent which will qualify him to argue on equal terms with those whose business it is to be expert in this branch of medicine. He should be able, however, to make some contribution in the light of his experience with splenectomy and particularly of surgery in general."[6]

This quotation from Edwards challenges surgeons to familiarize themselves with the indications for and the sequelae of splenectomy.

Unlike those diseases in which a certain diagnosis is an indication for a specific treatment, splenic disease is still identified symptomatically, and splenectomy often must be used in the hope of symptomatic relief, rather than in the certainty of relieving an underlying disease. Nevertheless, the surgeon should know which splenic functions he may alter or obliterature by splenectomy.

The first function of the spleen is hematopoiesis, which normally is present only during fetal life. In later life, though, if bone marrow is replaced by tumor, fibrosis or cortical bone tissue, so that normal hematopoiesis becomes impossible, the spleen reverts to its fetal function and becomes a source of formed blood elements. In this condition, known as myeloid metaplasia, splenectomy is contraindicated.

The second function is that of eliminating erythrocytes from the circulation, apparently by filtration. It is not clear how the normal senescent cell is affected by the spleen, since the life span of the erythrocyte (about 120 days[1]) is not prolonged after splenectomy.[15] More definite is the evidence in such blood dyscrasias as congenital spherocytosis. In patients with this disease who receive normal blood, the abnormal spherocytes are found in the spleen in far greater concentration than in the peripheral circulation. Conversely, if spherocytic blood is perfused through an essentially normal spleen (removed from a patient with thrombocytopenic purpura), the abnormal spherocytes are sequestered by the spleen. These findings demonstrate that the spleen does retain morphologically abnormal erythrocytes.

The third function of the spleen is to control bone marrow activity. Since depression of marrow function is relieved after splenectomy, it seems most likely that the spleen produces a hormone that has this depressing effect.

INDICATIONS FOR SPLENECTOMY

Hemolytic Anemia

Congenital hemolytic anemia has a number of descriptive names among which are: Hereditary spherocytosis, congenital hemolytic jaundice, familial hemolytic jaundice, acholuric jaundice, congenital hemolytic anemia, familial hemolytic anemia and spherocytic or globe-cell anemia. The spherocytic tendency is inherited as a Mendelian dominant and is characterized by abnormally thick red blood

From the Department of Surgery, College of Medical Evangelists, School of Medicine, Los Angeles 33.

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cells. These spherocytes are functionally adequate as to oxygen-carrying capacity, but their abnormal fragility and shape make them ever a prey to the splenic filter.[20,21] Splenectomy therefore both theoretically and in actual practice is a consistently beneficial therapeutic measure and good results can be expected in almost all cases in which diagnosis is clear-cut.

Splenectomy should be performed between acute hemolytic episodes, since operation is much better tolerated if the patient is relatively asymptomatic. This can usually be accomplished either by waiting or by the use of corticotropin (ACTH) or cortisone, and "emergency" splenectomy for congenital hemolytic anemia is rarely necessary.

Acquired hemolytic anemias may be divided into idiopathic and secondary. In the idiopathic acquired as well as in some of the secondary acquired types, the basic defect is a circulating antibody which causes spherocytosis with increased mechanical and osmotic fragility, resulting in hemolytic crises. The condition of the blood may thus appear superficially the same as in congenital hemolytic anemia, particularly during periods of hemolysis. The differential diagnosis is dependent upon two factors. One is the absence of familial incidence and the other is the presence of a circulating antibody which periodically attacks the red cells, causing excessive hemolysis secondary to abnormal shape and increased fragility. Between hemolytic crises, the red cell shape and fragility may be normal even though the antibody is still present. This antibody may be demonstrated in a large proportion of these cases by the Coombs test.[2]

Splenectomy benefits approximately 50 per cent of patients with idiopathic acquired hemolytic anemia, but predicting which will be benefited is quite difficult. If a patient is having serious symptoms, splenectomy should be offered if medical therapy, including use of corticotropin (ACTH) or cortisone, fails.[4]

The chief diagnostic differences between hereditary and acquired spherocytoses are summarized in Table 1.

The secondary acquired hemolytic anemias may be due to splenic involvement from lymphoma, leukemia, Hodgkin's disease, sarcoidosis, Gaucher's disease, kala-azar or tuberculosis. If the hemolytic anemia associated with any of these diseases is of prime importance and does not respond to medical measures, splenectomy may be of some benefit. It should be emphasized, however, that this is symptomatic therapy for hemolytic anemia and not a therapeutic measure for the underlying disease. The cause of this form of hemolysis is uncertain. It is postulated that in some cases in which the spleen becomes greatly enlarged, the organ elaborates a lytic substance which acts on the large amount of blood confined in it.

TABLE 1.—*Findings in Hereditary and Acquired Spherocytosis*[5]

	Hereditary	Idiopathic Acquired
Family history of disease	Usually present	None
Finding of disease in studies of family	Definitely positive	Negative
Abnormal antibody at body temperature	Negative	Positive
Result of Coombs test	Negative	Positive
Survival of transfused erythrocytes	Normal	Reduced

Thrombocytopenia

The basic defect in idiopathic thrombocytopenic purpura is arrest in maturation of the megakaryocyte which is the stem cell of the thrombocyte or platelet. The megakaryocyte fails to form the "buds" which in turn form the platelet.[14] In the majority of patients with idiopathic thrombocytopenic purpura, splenectomy is not necessary for amelioration of the symptoms. Most of the episodes either are self-limited or can be successfully treated with corticotropin or cortisone.[8] However, in some cases there is no response to conservative therapy, whereas 65 to 75 per cent of adults and 90 per cent of children respond well to splenectomy. After splenectomy, the megakaryocytes mature and form buds, and the platelet count increases. Simultaneously, the bleeding tendencies cease. There are observers who still maintain that the spleen acts as a filter of the thrombocyte in this disease; however, most of the evidence points to a humoral substance which arrests maturation of megakaryocytes by depressing bone marrow.

The diagnosis of idiopathic thrombocytopenic purpura usually is not very difficult, but secondary causes of thrombocytopenia must be excluded.[10,11] The essential diagnostic features of idiopathic thrombocytopenic purpura are a history of excessive bleeding or easy bruising, a platelet count of less than 100,000 per cu. mm. of blood, evidence of arrest in maturation of megakaryocytes, an absence of signs of bone marrow involvement by lymphoma, leukemia, or carcinoma, and a similar absence of systemic disease as determined by microscopic examination of peripheral blood. In the majority of cases, the spleen is not palpable in this disease. This finding alone will usually differentiate primary from secondary thrombocytopenia.

In general, secondary thrombocytopenia is a contraindication to splenectomy since it is part of the

systemic disease and splenectomy will be of no benefit. However, when excessive bleeding is a part of the systemic disease and cannot be controlled by the use of corticotropin or cortisone, splenectomy may be recommended and in some instances has controlled the bleeding and given the patient a more comfortable existence for the remainder of his life.

Hypersplenism and Cytopenia

The hypersplenic state may manifest itself through a reduction in all the formed blood elements (panhematocytopenia) or of any of these elements. An important although relatively infrequent deficiency is that of neutrophils (splenic neutropenia). Some investigators attribute this to active depression of bone marrow function such as occurs in idiopathic thrombocytopenic purpura; others believe it may be due to excessive phagocytosis by the spleen. Whatever the cause, splenectomy does result in an increase in leukocytes and freedom from infections secondary to neutropenia. The disease occurs most commonly in women 30 to 60 years old, who become chronically ill with recurrent skin and mouth infections. The spleen is enlarged and leukocytes number 1,000 to 2,000 cells per cu. mm. of blood. The bone marrow is excessively cellular, with many granular cells present although mature forms may be rare. In conjunction with this state, rheumatoid arthritis may be present (Felty's syndrome), but if splenectomy is recommended it should be for the leukopenia alone and not for the arthritis, on which it has no effect.

As previously stated, if all the formed blood elements are deficient, the syndrome is known as panhematocytopenia. In some cases, this may take the form of excessive destruction of blood, the symptoms being those of hemolytic anemia. In others, the deficiency seems to be due to depression of marrow function. As in other hypersplenic syndromes, the condition may be primary—and this responds well to splenectomy—or secondary, as a result of splenic involvement from lymphomas, Gaucher's disease, kala-azar or tuberculosis. The secondary state is less likely to respond to splenectomy, except in isolated instances when symptoms are due to size and malfunction of the spleen.[13]

ACCESSORY SPLEENS

One or more accessory spleens have been found in from 25 to 50 per cent of patients undergoing splenectomy. The possibility of this condition should be at least recognized by the surgeon.[3] Some investigators believe that accessory spleens may not be important; but the consensus is that they may cause the disease process to continue or recur, and therefore should be removed.[12,19]

Three out of four accessory spleens are found in the hilar or pedicle area of the spleen. These present no problem in visualization and removal. More troublesome are the minority found in locations which may seem puzzling until the embryonic development of the spleen is considered. In the twelfth week after conception, the spleen is a differentiated structure situated between the mesonephric and the urogenital folds. During the caudal migration of the genital gland, splenic tissue may be carried along, to be deposited at the upper pole of the left testis and epididymis, or, in females in the region of the left mesosalpinx and mesovarium. The path of migration is in some cases evident in a band of fibrous or splenic tissue, or both, connecting the normal spleen with the ecotopic tissue in the scrotum or the broad ligament. Before splenectomy, the scrotum should be carefully examined in males; in females the entire abdomen including the left adnexa should be searched for accessory spleens. If the postoperative result is not satisfactory, the possibility of accessory spleens should be considered.

SEQUELAE

Most reports on splenectomy make no reference to any untoward sequelae. Some investigators believe that at a given degree of platelet surplus, heparin or some other anticoagulant should be given to obviate thromboembolic disease, but others consider this precaution unnecessary. Since it is known that if all the other clotting elements in the blood are normal an increase in platelets increases coagulation, it seems reasonable that any increased danger should be met by antithrombotic measures.

In recent years there has been an increase in reports of infections in children following splenectomy. In 1952 King and Shumacker[9] reported case histories of five infants under six months of age who had multiple infections following splenectomy. The indication for splenectomy in all these infants was congenital hemolytic anemia. Four of the five infants had either meningitis or overwhelming meningococcemia in from six weeks to three years after operation, and one of the four died of the infection. The fifth child was returned to the hospital a few days after discharge following splenectomy with a rapidly fatal febrile illness, apparently infectious in nature. In 1955, though, Walter and Chaffin[18] reported on ten infants from the Children's Hospital in Los Angeles who had had splenectomy below the age of 7 months; in this group there was no increase in the infection rate. At the Children's Hospital in Boston an increased incidence of pneumococcic infections in infants occurred following splenectomy, and a similar observation was made by Smith in New

York.[16] The cause of this increased rate of infections is not clear, especially since it has been shown that the gamma globulin fraction is not decreased in infants after splenectomy. Nevertheless, children should be observed closely for infections after splenectomy so that therapy can be instituted at an early date if there is any indication of infectious disease.

There appears to be no increase in infections in adults following splenectomy.

540 North Central Avenue, Glendale 3 (Joergenson).

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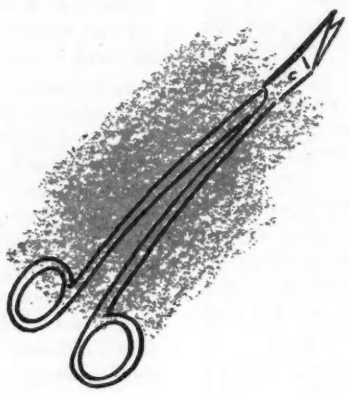

Hypersensitivity to House Dust

A Preliminary Report on Treatment of Children with Antigens at Two Different Dosage Levels

WALTER R. MacLAREN, *M.D.*, Pasadena, and GENE HABER, *M.D.*, Los Angeles

• **Two comparable groups of children with allergic sensitivity primarily to house dust were treated respectively with low (1:1,000,000) and high (1:100) dilutions of Endo house-dust extract. In the two groups there were 47 patients with asthma, 5 with chronic allergic rhinitis, and 10 with both.**

After an average of 16 to 18 months of injection treatment, good to excellent results were obtained by 75 per cent of the patients on low dosage and 80 per cent on high dosage. Change of dosage from low to high in five cases, and from high to low in five others, made no perceptible difference in results. Continuous and regular treatment seemed to be more important than the size of dose.

The apparent effectiveness of small doses of dust extract may be due to the polysaccharide nature of the material which persists as an active antigen in the tissues.

SENSITIVITY TO HOUSE DUST as shown by clinical history and skin testing is the commonest finding among patients referred to the Allergy Clinic at the Los Angeles County General Hospital. This form of allergic sensitivity accounts for many cases of chronic asthma and rhinitis in children and adults, and there is good reason to believe it is often a major factor in cases of persistent atopic eczema.

Statements in the literature, in textbooks and from practicing allergists show a good deal of divergence of opinion as to the proper dose of house-dust antigen to use in treatment. Feinberg[1] for example suggested that the use of a potent extract such as Endo house-dust antigen begin at 1:1,000,000 or 1:100,000 dilution and be increased as high as 1:40; "the chance of obtaining good results is usually much better when attempts are made to reach a maximal dose," he said. Hansel[2] on the other hand advocated much greater dilutions, in the range of 1 to a million million to 1:1,000,000 in cases of severe asthma.

The study here reported was undertaken to see what difference could be demonstrated in clinical results between two groups of children equally sensitive to house dust, one of which was treated with the weakest dilution of this antigen used in our clinic, the other with the strongest. This represents a 10,000-fold difference in amount of injected antigen.

SUBJECTS

Sixty-two children attending the Allergy Clinic cooperated in this study—32 receiving the low dose of antigen, 30 others the high dose. Children were assigned more or less in rotation to the two groups, with minor variations to keep the two groups as closely comparable as possible. The pertinent characteristics of the two groups are given in Table 1. Only children responding primarily to house-dust antigen on scratch and intradermal tests were included in this study. Forty children gave 4-plus reactions, 19 gave 3-plus, and three gave 2-plus when tested intradermally with Endo house-dust antigen at 1:1,000 dilution. Six children reacted moderately to other inhalant household allergens, and 13 reacted slightly or moderately to one or more pollens. None of the children had typical pollen allergy alone, though three had spring or summer exacerbation of chronic allergic rhinitis.

PROCEDURE

Severity of the asthma before treatment was judged in terms of hospitalization for acute attacks, the amount of medication required, interference with school attendance, and physical evidence of dyspnea and its results. About 70 per cent of the subjects were considered to have severe (4-plus) symptoms before starting treatment.

During treatment, the patients' clinical state was graded weekly: A rating of 0 indicated there was no asthma and no treatment other than routine desensitization injections; 1 indicated occasional mild attacks that did not limit activity and were treated with minor oral medication; 2 indicated some interference with normal activity, and 4 designated severe asthmatic attacks. From these ratings, an average was compiled by totaling the rating figures and dividing by the number of visits. This average,

From the Department of Medicine (Allergy) of the University of Southern California School of Medicine, and the Allergy Clinics, Los Angeles County General Hospital.

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compared with the patient's own estimate of improvement, was the basis for the overall assessment of results.

Endo house-dust extract was used in treatment. This extract is prepared from mixtures of house dust collected in various parts of the country. The active material is concentrated by precipitation and standardized biologically for reasonable uniformity from batch to batch. Children on low dosage were given weekly injections of .05 cc. of 1:1,000,000 dilution throughout the study. Children on high dosage were started on the same amount, but the dose was increased to .05 cc. of 1:100 dilution in 18 to 24 weekly steps. The rate of increase was governed by individual tolerance. Local reactions to increasing doses occurred frequently, but none was severe enough to stop treatment. The final dose of .05 cc. of 1:100 dilution was continued throughout the period of treatment.

The effect of treatment was counted from the third month of low dosage, and in the high-dose group from the time a 1:1,000 dilution of dust antigen was reached. The average duration of treatment was 16 months for the low dosage, 18 months for the high. All the children on high dosage tolerated the 1:100 dilution, except one who began to have asthma following each injection after nearly a year on treatment, and therefore was reduced to low dosage, on which he did well.

For the sake of comparison, five other children who had been receiving high dosage were reduced to low dose for a considerable period, and for four others the dosage was increased from low to high.

TABLE 1.—*Characteristics of Two Groups of Children, Sensitive to House Dust, Treated with Low and High Dosage of House-Dust Extract*

	Low-Dose Group	High-Dose Group
Diagnosis:		
Asthma	26	21
Asthma and allergic rhinitis	4	6
Allergic rhinitis	2	3
Total cases	32	30
Sex distribution:		
Boys	21	18
Girls	11	12
Severity of major complaint:		
++++	22	24
+++	8	5
++	2	1
Age at start of symptoms:		
Range	1 to 9 yr.	1 to 11 yr.
Median	2 yr.	2 yr.
Age at start of treatment:		
Range	3 to 11 yr.	3 to 11 yr.
Median	7 yr.	8 yr.
Median duration of major complaint	5 yr.	5 yr.

TABLE 2.—*Results in 62 Children Sensitive to House Dust Who Were Treated with High and Low Dosage of House-Dust Extract*

Diagnosis and Clinical Result	Low-Dose Group		High-Dose Group	
	No. Cases	Per Cent	No. Cases	Per Cent
All asthma cases:				
Excellent	7	23	5	19
Good	15	50	16	59
Fair	6	20	4	15
Poor	2	7	2	7
All cases:				
Excellent	7	22	7	23
Good	17	53	17	57
Fair	6	19	4	13
Poor	2	6	2	7
Duration of treatment:				
Average	16 mo.		18 mo.	
Minimum	8 mo.		8 mo.	
Maximum	24 mo.		24 mo.	

RESULTS

As indicated in Table 2, good to excellent results were obtained in 73 per cent of the asthmatic patients on low dosage, and in 78 per cent on high dosage. For all patients, including those with rhinitis, the figures were slightly higher—75 per cent good to excellent results on low dosage, 80 per cent on high dosage. Thus a slight advantage might be ascribed to high dosage, but in so small a group it is doubtful, in view of the variables involved, that the difference is significant. When all cases on each regimen are compared, there appears to be no real difference in the therapeutic result. Further analysis revealed no difference that might be ascribed to the age at which treatment was begun, the severity of symptoms before treatment, or the degree of sensitivity to dust antigen. As noted above, the results with the five children shifted from low to high dosage was exactly the same as for the five shifted from high to low dosage: Four were unaffected, one was slightly worse.

The three children who reacted to pollen tests as well as to dust, and who were subject to seasonal exacerbation of symptoms, were noticeably better during their bad seasons even though treated with house-dust antigen alone—presumably because their overall allergic load was decreased.

DISCUSSION

It is apparent from these observations that, in the range of doses used, there is no direct relationship between the amount of dust antigen given and the therapeutic result. That is, greatly increasing the amount of antigen does not increase the degree of

relief significantly. This may be due to the fact that the smaller amount of antigen saturates the antibody-producing mechanism, so that any larger amount is not utilized. The response to very much smaller amounts of antigen, in the order of several million-fold dilutions of the standard extracts, is now being measured on a new group of dust-sensitive children. This may show the degree of response as related to the antigen at various dosage levels and the saturation point at which response does not increase with an increase in dosage.

Approximately one-quarter of the children did not respond well to desensitization. It may be that they have a much higher requirement of antigen, or they may be deficient in forming "blocking antibody." Further work is necessary to show how antibodies against dust are produced.[3] It was also apparent from the records of these and other children not included in the study that in most cases where improvement was not obtained, treatment had been irregular or infrequent. Regular injection treatment at weekly or bi-weekly intervals appears to be of considerable importance in controlling dust sensitivity.

Reports on treatment of pollen-sensitive patients indicate that best relief is obtained by the use of as large an amount of antigen as the patient can tolerate.[4] The different behavior of the dust antigen may be due to its nature as a polysaccharide. Polysaccharide antigens from bacteria are known to remain in the body and be antigenically active for long periods. The same concept may be extended to the dust antigen. If the body cannot destroy this readily after injection, small amounts given frequently could soon produce a reservoir adequate to stimulate maximal production of blocking antibody.

136 North Madison Avenue, Pasadena (MacLaren).

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Social Security Footnotes

SINCE BISMARCK introduced socialized medicine in Germany three-quarters of a century ago, the threat of socialized medicine through the extension of so-called social insurance has been ever-present in western civilization. One nation after another has succumbed to the drive to extend the compulsory system of taxation called social insurance to finance a vast program of medical and hospital care for taxpayers and nontaxpayers. The history of developments in this field in foreign countries should alert the medical profession to the usual consequence of federal social security program.

—From the Department of Public Relations, American Medical Association

Resuscitation of Newborn Premature Infants

A Clinical Study of the Use of Positive Pressure Respiration

MIRIAM G. WILSON, *M.D.*, and
STANLEY N. ROSCOE, *Ph.D.*, Los Angeles

• **The Goddard-Bennett-Lovelace hand resuscitator was used for initiating respiration in 87 newborn infants with respiratory difficulties, during a five-month period at the Los Angeles County General Hospital. On alternate days, when the respirator was not used, 126 comparable infants received resuscitation by mouth-to-tracheal pressure and other means. Neither term infants nor previable infants benefited by use of the hand resuscitator, but premature infants weighing more than 1,000 gm. had a definite advantage, with a mortality of only 13 per cent for those treated with the resuscitator against 34 per cent among the controls.**

Neither roentgen nor postmortem studies of the lungs disclosed any consistent effect of any resuscitative measure employed.

POSITIVE PRESSURE is being widely used in resuscitation of the newborn. The simpler methods—mouth-to-mouth or mouth-to-catheter breathing—are thought to be hazardous because the pressure is uncontrolled and may easily be excessive, and because the infant's respiratory tract is unavoidably contaminated. Tracheal catheterization itself adds another danger unless done by a skilled operator, especially if the infant is very small. Most of the positive pressure resuscitators that are commercially available use pressures of less than 20 cm. (water). According to Day and co-workers,[3,6] a pressure of 40 to 60 cm. is necessary to expand the newborn atelectatic lung, and is safe if applied for no more than 0.2 to 0.5 second. Other investigators have demonstrated that positive pressure applied within these limits, and with a controlled volume of air, is clinically safe.[1,4] However, there has been no controlled study to demonstrate the value of such resuscitation for asphyxiated newborn infants, although respiratory difficulty causes 30 to 50 per cent of the deaths among newborn infants and at least 50 per cent among premature infants, many of whom have no other serious abnormality.

At the Los Angeles County General Hospital the authors attempted to evaluate the use of the Goddard-Bennett-Lovelace (GBL) infant hand resuscitator, with which the operator, after brief experience, can learn to regulate the duration of the positive pressure impulse within the safe range of 0.2 to 0.4 second. According to the inventors, the lung alveoli

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From the Department of Pediatrics, University of Southern California Medical School, Los Angeles County General Hospital. This study was supported in part by funds from the Attending Staff Association of the Los Angeles County General Hospital.

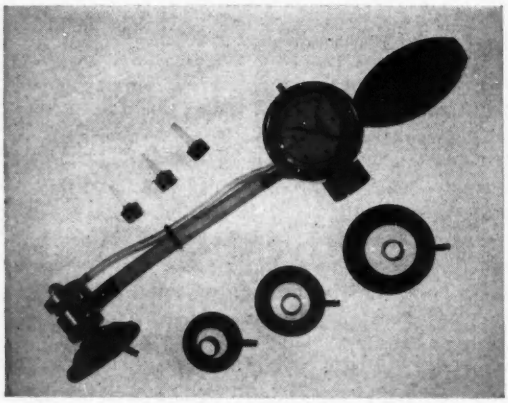

Figure 1.—The Goddard-Bennett-Lovelace (GBL) infant hand resuscitator. Tracheal catheter attachments are pictured to the upper left of the resuscitator and additional masks to the lower right.

Figure 2.—The Goddard-Bennett-Lovelace resuscitator in use. Note the hyperextension of the infant's head and the tight fit of the mask.

of newborn infants can be uniformly expanded by a pressure of 60 cm. (water) applied for 0.2 second. Overexpansion, they found, was not microscopically evident until a pressure of 80 cm. had been applied, and gross rupture might occur at 95 cm.[4] Among the 21 infants in one study[5] who were examined postmortem after unsuccessful treatment with the CBL respirator, only one had lung damage due to overexpansion—and in this case positive pressure at 60 cm. of water had been used for an hour after death in an attempt to revive the infant. In practice, pressure this high is needed only for initial expansion of the lungs; once they are partly expanded, much lower pressure is adequate.

Emphasis should be placed not on the degree of lung expansion obtained by any method, but rather on establishing an adequate air exchange by whatever degree of expansion makes this exchange possible. In many newborn infants who have apparently begun to breathe normally, roentgen or postmortem study may reveal some neonatal atelectasis. Wilson[9] has called attention to another danger difficult to determine clinically: If a large proportion of the lung is unexpandable because of pronounced atelectasis, accumulation of fluid or obstruction, there is greater risk of rupturing the lung with positive pressure.

EQUIPMENT AND USE

The Goddard-Bennett-Lovelace (GBL) infant hand resuscitator* is intentionally a simple device consisting of a hand bulb, positive pressure gauge, a pressure control knob, an oxygen or room air inlet and a mask or tracheal catheter attachment (Figures 1 and 2). A practice meter is also included so that the operator may become accustomed to deliver a machine-determined pressure over a time interval of 0.2 to 0.4 second.

The obstetrical residents used the apparatus only as a resuscitator and only within the delivery rooms. It was not used after the immediate newborn period in the nursery wards. The operators were instructed to use oxygen at high concentrations, on the principle that in brief application the lifesaving value of oxygen is more important than the remote possibility of influencing retrolental fibroplasia. A flow of 10 liters per minute was estimated to provide an oxygen concentration of 60 per cent. A pressure of 40 to 60 cm. water was applied intermittently at 40 to 60 impulses per minute (within the 0.2 to 0.4 second limit), and after each three minutes the treatment was interrupted for from 30 seconds to a minute. After 5 minutes, total time, pressure was reduced to 20 to 30 cm.

*Manufactured by V. Ray Bennett and Associates, Inc., 320 S. Robertson Blvd., Los Angeles 48.

PLAN OF STUDY

The controlled study was designed to demonstrate what value the infant resuscitator might have when used in addition to standard methods of resuscitation. Control and experimental periods consisted of alternate 24-hour intervals in all delivery wards except the isolation and prison wards. Standard methods for treatment of asphyxiation in the newborn were used in both periods, the only difference in the experimental periods being the use of the resuscitator. As far as possible, rotation of obstetrical residents assured that professional competence was equal for the alternating periods, but no resident used the respirator until he was practiced with it. Most of the residents worked in both the control and the experimental periods.

All infants included in this presentation were liveborn. Any infant requiring further stimulation to breathing than ammonia whiffs and oxygen was considered to have had resuscitative therapy. Routine care immediately after delivery included warm blanketing, nasal and pharyngeal aspiration by bulb syringe, and postural drainage. In addition, at the resident's discretion, postural drainage might be prolonged, the trachea aspirated, mouth-to-tracheal pressure applied by catheter, and stimulants administered—ordinarily caffeine or epinephrine, but sometimes Nalline® as an antidote to morphine or its derivatives administered to the mother before delivery. All infants receiving any kind of resuscitative therapy were given penicillin and streptomycin parenterally for three days*; otherwise, their care was routine unless other conditions required treatment.

RESULTS

During the five-month period of the study, 3,087 children were born on control days, 2,642 on experimental days. In each group there was a normal proportion of premature deliveries—281 among controls, 246 among the experimental group. The distribution of weight was also normal (Table 1). Of all the infants in the study, 213 or 3.7 per cent required resuscitation. This is a low proportion compared with those reported from other hospitals, but the disparity may be due to differing definitions of resuscitation. In the control group, 82 term infants and 44 premature needed resuscitation; in the experimental group, 59 term infants and 28 premature (Table 2).

One discrepancy appears in comparing the control and experimental groups among premature infants weighing more than 1,000 gm. (Table 3). Among the 267 controls, 41 (about 15 per cent) were considered in need of resuscitation. For the 237 in the experimental group, only 24 (a little over

*Penicillin and streptomycin are now not given routinely in these circumstances.

TABLE 1.—*Incidence of Premature Infants in Each of Four Weight Ranges at Los Angeles County General Hospital During Respirator Experimental Period*

Weight in Grams	Number of Premature Infants: Control	Experimental*	Chi²†	P†
1,000 or less	14	9	1.398	0.24
1,001 to 1,500	23	22		
1,501 to 2,000	58	59		
2,001 to 2,500	184	155		

*Two other infants in the control group and one in the experimental group were not weighed and are not included in this tabulation.

†Mathematical method of determining probability (P).

TABLE 2.—*Attempts at Resuscitation of Term and Premature Infants at Los Angeles County General Hospital During Respirator Experimental Period*

	Number of Cases	Number Treated	Chi²†	P†
Term Infants:				
Control	2,806	82	1.056	0.36
Experimental	2,396	59		
Premature Infants:				
Control	281	44	2.033	0.16
Experimental	246	28		

†Mathematical method of determining probability (P).

TABLE 3.—*Attempts at Resuscitation of Premature Infants Weighing More Than 1,000 Grams*

	Number of Cases	Number Resuscitated	Chi²†	P†
Control	267	41	3.056	.08
Experimental	237	24		

†Mathematical method of determining probability (P).

TABLE 4.—*Mortality Among Premature Infants Weighing Over 1,000 Grams for Whom Resuscitation Was Attempted*

	Number of Cases	Number of Deaths	Chi²†	P†
Control	41	14	3.673	0.06
Experimental	24	3		

†Mathematical method of determining probability (P).

TABLE 5.—*Mortality of Term Infants for Whom Resuscitation Was Attempted*

	Number of Cases	Number of Deaths	Chi²†	P†
Control	82	9	0.223	0.65
Experimental	59	8		

†Mathematical method of determining probability (P).

TABLE 6.—*Types of Resuscitation Techniques Used During Experimental Period*

Types	Number	Per Cent
Control period (126 patients):		
Tracheal catheter	114	91
Stimulants	41	32
Artificial respiration	9	7
Experimental period (87 patients):		
GBL‡	67	78
With tracheal catheter	30	....
Without tracheal catheter	37	....
Tracheal catheter (without GBL)	15	17
Stimulants	18	21
Artificial respiration	9	10

‡Goddard Bennett-Lovelace resuscitator.

10 per cent) were so treated. It appears quite likely that some factor in the experimental situation deterred the residents from employing resuscitation so freely when the resuscitator was available as when it was not.

A significant improvement in survival was obtained by use of the respirator on premature infants weighing more than 1,000 gm. (Table 4). Among the 41 controls, 14 (34 per cent) died; among the experimental group, only 3 out of 24 (13 per cent).* There is only one chance in about 17 that this difference between the groups was accidental.

No such benefit was demonstrated for term infants (Table 5). Of 82 in the control group treated by respirator, 9 (11 per cent) died; of 59 in the experimental group, 8 (14 per cent) died. In these small numbers the difference is not significant.

Nor were the chances of previable infants improved by use of the respirator, which did not save any of these infants on whom it was used.

Quite obviously, resuscitation methods could not be sterotyped in either the control or the experimental groups. An attempt to subdivide the groups according to the various methods employed would result in a number of categories, none of which could be legitimately compared with the others. The proportionate use of these methods was largely dictated by the sequence in which they were applied until spontaneous breathing was established (Table 6).

As might be anticipated, a high proportion of the infants requiring resuscitation had been affected by maternal and obstetrical abnormalities, and there was high morbidity in the neonatal period—congenital malformations, associated birth injuries, and illnesses severe enough to require hospitalization in the first three months of life. Thirty-two such cases were counted, but the number was probably larger, for return of patients for examination after discharge is notoriously poor in county hospitals.

Neither roentgen nor postmortem studies of the lungs revealed any consistent effect of positive pres-

*All deaths in this study occurred in the first week of life.

sure respiration by any method employed. Of the 103 chest films made, 70 per cent showed the lungs normal. Certain infants who had been treated with the respirator for long periods or at relatively high pressures had no roentgen signs of overexpansion; for example, of three infants treated for 15 minutes at 40 to 50 cm. (water), only one had what was thought to be slight overexpansion. Of four others who had received a pressure of 60 cm., two had an essentially normal roentgen appearance of the lungs; one (treated for only a minute) had "patchy atelectasis" and overexpansion of the thoracic cage; in the other, after 10 minutes' resuscitation, expansion was still decidedly incomplete. In the control series, likewise, the roentgen appearance did not correlate well with the length of time that mouth-to-trachea pressure had been applied by catheter. No roentgen study disclosed any evidence of pneumothorax or of mediastinal or subcutaneous emphysema. All these films were studied by a single roentgenologist who had no information as to the type of resuscitation employed.

Postmortem examination of the lungs revealed dangerous overexpansion in one infant, who had rupture of the visceral pleura after 45 minutes of positive pressure with the respirator. The primary cause of death was extensive atelectasis and hyaline membrane formation. This child did not breathe spontaneously at any time, and resuscitation had been continued until the heartbeat ceased. Other postmortem studies indicated that positive pressure of any type could result in overexpansion of certain portions of the lungs. Infants who had had difficulty in beginning respiration, with or without positive pressure treatment, had patchy areas of atelectasis and interstitial emphysema. Subpleural emphysema was found in some who had had either orotracheal or mechanical pressure treatment for periods of a minute to an hour.

DISCUSSION

Theoretically, a premature infant weighing over 1,000 gm. should benefit most from improved resuscitation techniques, since faulty aeration is frequently the only problem. Term infants requiring resuscitation may have major disorders causing the respiratory difficulty, or may have severe asphyxia related to birth processes. Premature infants weighing 1,000 gm. or less may be arbitrarily considered previable, since many are biologically unable to support life in an extrauterine environment regardless of the type of resuscitation. The findings in this study agreed with these theoretic considerations.

An interesting observation is the more frequent use of resuscitation in the control group of infants. After reviewing the individual cases, the authors believe that more resuscitation occurred in the control periods because the residents had more flexibility of schedule. For example, on control days, the residents could administer a stimulant if the infant seemed only slightly depressed. The residents in the experimental periods, on the other hand, were encouraged to use the resuscitator as soon as possible and to avoid other methods until after the resuscitator had been used. Therefore infants who were thought to be merely "sleepy" were usually not resuscitated although if they had been seen in the same condition on a control day, they might have been given stimulants. In practice, therefore, since there was a tendency in the control periods to resuscitate infants who were in less need of resuscitation, the advantage in survival rate of the experimental resuscitated group becomes more striking.

If an easily used resuscitator offers an advantage in a large maternity center where the medical staff is prepared for emergency situations and is well trained in the use of current resuscitation techniques, such a resuscitator might be expected to be even more advantageous in a small hospital where resuscitation is an unusual and consequently a less efficiently managed procedure.

241 North Figueroa Street, Los Angeles 12 (Wilson).

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Musculoskeletal Complications of Hemophilia

ELLIS W. JONES, M.D., Pasadena

• **Persons with hemophilia may be crippled by hemorrhages into soft tissue, the pressure destroying nerve and muscle. Recurrent bleeding into joints produces severe arthritis with synovitis and damage to cartilage and bone. The resulting deformities, even of long standing, may be greatly lessened, so far as impairment of function is concerned, by conservative orthopedic treatment. Treatment also may slow the progress of crippling deformities.**

MANY PHYSICIANS rarely see hemophiliac patients. When they do, they apparently tend to undertreat them, lest they do more harm than good. This paper presents nothing new, but is a review of musculoskeletal problems associated with hemophilia that have been observed by the author and a report on how these problems were dealt with. The joint destruction, the contractures and the paralysis of hemophiliac patients resemble arthritis, club feet and poliomyelitis and are often amenable to the same care. Surgical treatment, of course, is out of the question, but conservative orthopedic measures are sometimes a boon.

Several investigators—Ghormley and Clegg,[6] Thomas,[14] Caffey and Schlessinger[2] and others*—have written excellent reviews of the problem of hemophilic arthritis, but that their work may not be sufficiently well known is indicated by the number of patients observed with crippling deformities which have never been treated, although they might have been held to lesser degree had they been dealt with in the early stages. Indeed, many such patients have improved significantly even with delayed care.

There are 242 hemophiliac persons registered with the Southern California chapter of the Haemophiliac Society. One hundred and ten, or 45 per cent, are patients with musculoskeletal disorders resulting from the disease. It is with them that this paper is concerned. With the exception of one case of paraplegia, which occurred subsequent to a spinal puncture, I have not seen involvement of the spine, and my experience has been entirely with disorders of the extremities.

The problems are both acute and chronic, the latter being the more difficult to manage over a long period.

ACUTE PROBLEMS

Hemorrhage

Control of bleeding by reducing the clotting time is an emergency measure.[16] Hemorrhage can arise spontaneously as well as from various degrees of trauma. Hematologists do not agree upon details of measures necessary to reduce the clotting time. In the majority of cases I administer Hyland Laboratories' antihemophilic plasma in a dose of 1 to 2 cc. per pound of body weight. In 1956, 2,041 liters of plasma and 174 units of whole blood were administered to hemophiliac persons registered with the Haemophiliac Society in our area, including those with visceral bleeding. Plasma is supplied without charge to all patients. Those living at a distance keep it in their refrigerators for administration by a local physician.

Fractures

Fractures are treated by the orthodox methods of traction, splinting and casting. Sometimes breaking a bone causes more bleeding in a hemophiliac than in a normal person, but usually the hematomas are not large as compared with some of the larger ones that occur in soft tissue after considerably less trauma than that needed to break a bone. Theoretically, traumatic damage to tissue engenders a substance necessary in clotting.[5]

Hematomas associated with fractures in hemophiliac patents should not be aspirated or evacuated, for the puncture or incision would be hazardous. Circular casts are not applied until swelling has subsided and early healing of the bone is established. Open reduction is out of the question; deformity is more acceptable. Bone healing occurs at a normal rate, usually with abundant callus.

Soft Tissue Bleeding

Bruises often remain small but can grow insidiously into enormous crippling hematomas, and each one must be watched. Patients gain experience with their own bleeding problems, which differ in each case and at various times. They often can forecast quite accurately the likely extent of a hemorrhage.

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From the Department of Surgery (Orthopedics), University of Southern California School of Medicine.

*7,11,12,13,17

Figure 1.—Swollen knee resulting from recurrent intra-articular hemorrhages. Note striae.

It is to be emphasized, however, that; when doubt exists, efforts to stop the bleeding should be started immediately. In addition to lowering the clotting time by the administration of antihemophilic plasma, these measures consist of absolute rest of the part and packing the area of hemorrhage in ice. This is best done in the hospital where the swelling can be observed and nursing care and drugs are available for control of pain and restlessness.

Bleeding into Joints

Minor leakage of blood into a joint is rare. When hemorrhage develops in a joint the joint usually distends to full capacity until the intra-articular pressure is as high as the systolic pressure and no more blood can be pumped in. More may leak in, however, as the initial hemorrhage absorbs, a process which may continue indefinitely.[8] Patients with intra-articular hemorrhages should be put in hospital for care in order to minimize permanent damage (see Figure 1). Bleeding into a joint is usually very painful, a symptom useful to distinguish it from the lesser discomfort of the relatively less serious bleeding adjacent to a joint.

Deformity also requires treatment. I use plaster shells for elbows, wrists and ankles, splinting the elbow at a right angle, holding the wrist in the position of function and splinting the ankle at a right angle to prevent foot drop. For hip and knee joints, Russell traction or Buck's extension is used, the patient wearing a padded tennis shoe. Traction should not be used to try to correct the contracture but should pull in the line of the deformity and be adjusted daily as muscle spasm subsides.

Even though recognizing that the presence of free blood in a joint may do severe damage to it, I consider aspiration in such circumstances unwise, for the trauma of the needle may produce further bleeding even after the clotting time has been brought to normal. I have not had experience in the injection of hyaluronidase in an effort to speed absorption of blood.[1,9]

Addiction to Narcotics

As with many chronic diseases, the danger of addiction is always a factor in dealing with the painful concomitants of hemophilia. Many hemorrhages, particularly intra-articular, are so painful as to make the use of narcotics necessary for relief. Some of the patients I have treated were already addicted when first observed, narcotics apparently having been the only previous treatment.

THE PROBLEM OF CHRONIC DISABILITY

The chronic disabilities of hemophilia—muscle weakness and paralysis, contractures, synovitis and degenerative arthritis — are a major orthopedic problem.

Weakness and Paralysis

Muscle weakness arises either because of nerve damage resulting from pressure of a hematoma in a closed fascial space or from disuse of an extremity. I treat it as though it were the muscle weakness of poliomyelitis, using electrical stimulation and exercises to restore strength, and braces for support and the control of antagonists. The quadriceps is the most commonly weakened muscle, usually as the result of chronic hemophilic arthritis in the knee joint but sometimes because of damage to the femoral nerve by groin hemorrhage. Volkman's contracture and peroneal palsy sometimes occur.

Contractures

Contractures of hips, knees, feet and ankles respond well to traction, braces and, occasionally, wedging plasters, along with muscle reeducation. Gentleness is essential. These joints will bleed if quickly forced. The knee is the most frequently involved (Figure 2). I have used adjustable long-leg braces successfully to overcome knee joint flexion contractures of long standing. The patient is permitted to walk despite the deformity, but a posterior bar on the brace blocks further flexion while the leverage of the brace gently urges further extension with each step. As the contracture diminishes, the brace is adjusted gradually until the knee reaches full extension, when free motion is started.

Improvement can be brought about in "frozen" shoulders by using the customary measures of x-ray therapy to control pain, then heat, massage, stretching and exercise.

Figure 2.—Fixed knee flexion contractures resulting from untreated recurrent joint bleeding.

Figure 3.—X-ray film showing advanced hemophilic arthritis of knee in a 14-year-old boy, characterized by erosion articular surface, lipping of joint margins, subchondral bone cysts.

Synovitis

Unfortunately, the majority of contractures are complicated by various degrees of synovitis and articular damage resulting from a series of hemorrhages. The prognosis for full recovery of these joints is poor, but worthwhile functional improvement can be obtained.

Experimental evidence has been reported that synovial hyperplasia[10] and subsequent hemovillous villonodular synovitis[18] can result from repeated hemorrhage. Hyperplastic synovitis can be reduced, but treatment has been disappointing in the few patients suspected of having villonodular synovitis with whom I have dealt. Treatment of arthritic joints is the treatment of the contractures plus an attack on the synovitis. For this I use hydrocortone intra-articularly, x-ray therapy and prednisone (Meticorten®) by mouth. The number of patients so treated is too small for statistical conclusions, but the results of all three forms of treatment have been encouraging.

Hydrocortone is injected intra-articularly, after the clotting time has been reduced to normal by infusion of plasma. This produces significant relief of pain and clinical improvement in synovial thickening and fluid. It has not restored a joint to normal in any case observed.

X-ray therapy has produced varying degrees of improvement in about 80 per cent of patients with chronic synovitis. It has been particularly helpful in reducing the swelling and pain and increasing the range of motion in elbow joints. The clinical improvement, however, has not always been as evident as the patient's gratifying relief from pain. Lest epiphyses be damaged, x-ray therapy has been reserved for adults only.

I have used oral Meticorten in 14 patients with multiple joint involvement. All of them have reported decided diminution of pain and improvement in their sense of well-being. Moderate improvement in the joints has been observed clinically. How long Meticorten therapy can be continued and precisely what the dose should be cannot be said as yet.

Osteoarthritis

Although we have no method of direct attack on damage already done to bone and cartilage,[3] treatment of weakness, contractures and synovitis often can restore a badly damaged useless joint to useful function. I believe treatment of this kind also can decrease the rate of further degeneration. I believe that treatment of the acute episodes of hemorrhage and care of the deformities will at least postpone crippling.

The roentgenographic appearance of osteoarthritis (Figure 3) sometimes resemble the changes seen in rheumatoid arthritis and tuberculosis. Typically, there is narrowing and roughening of the joint spaces, increased opacity of the soft tissues due to deposition of iron pigments, osteoporosis, epiphyseal cysts and spurring at the epiphyses.

47 Congress Street, Pasadena.

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Brain-Damaged Children

The Problem of Relations in the Family Group

EDMUND F. WALKER, *M.D.*, and DAVID L. KATZ, *M.A.*, Los Angeles

• **Children with minimal brain damage show a characteristic pattern of behavior.**

Often there are no physical signs of abnormality, but the diagnosis can be made from the history, electroencephalographic tracings, psychologic tests and repeated observations.

The behavior is a composite of the effects of the brain damage and the response of the child to his environment. The behavior of the brain-damaged child is frequently so frustrating to parents that attitudes of rejection, withdrawal or excessive punitive measures occur.

In the present study, when drugs were given and the child's behavior improved, the parents were better able to understand the needs of the child and create a better home environment in which there was less frustration and emotional pressure.

INCREASING ATTENTION has been centered recently on children's behavior disorders which are the result of damage to the brain. The rapid progress of late in neuropharmacology, neurophysiology and neurosurgery give promise that this will be more than a mere matter of academic interest and will lead to the organization of a more effective treatment program. No one would deny that the brain is the organ of the mind, and few would deny that a better understanding of the various functions and processes of the brain is basic to an understanding of mental functioning in health and in disease.

It is equally accurate to state that no behavior occurs in a social vacuum. Behavior and behavior abnormalities must also be understood in terms of the child's attempts to fulfill his normal physical, intellectual, social and emotional needs. The interplay between child and parents, child and school, siblings and peers, all make their contribution to the forces which produce his total behavior.

It is accepted that repeated or severe frustration in a child's effort to attain satisfaction for these needs will result in a series of defensive patterns which can range from a simple situational reaction to a psychotic break. A child's resources for attaining satisfactions for these needs come not only from his environment but equally come from within himself. This general formulation would apply as well to the adjustment of a child with brain injury as to the child without damage. From this point on, however, there are certain important differences existing in the child who has brain damage. These fall in three categories: (1) Certain of his needs are different and greater than with other children; (2) his capacities to attain satisfaction from his environment are decreased; (3) the symptoms he has tend to alter the attitudes of family, school, siblings, and playmates making it difficult or almost impossible for him to attain satisfaction in his relationships with this group.

In the present communication, attention will be limited to brain-damaged children who would be classified as having minimal injury.

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While many of the behavioral deviations of a child with minimal brain injury have been ascribed to external environmental factors, there remains a group of children showing behavioral response of a specific type. This behavioral response is variable in its intensity, and the brain damage may be so minimal or benign as to be considered normal individual differences or ascribed vaguely to inherent constitutional characteristics. The behavioral syndrome of the child with organic brain disease has been adequately described by Bradley,[3] Bender,[2] Bakwin,[1] Milman[4] and others. Strauss and Lehtinen[5] carried out thorough and searching studies particularly in relationship to the educational problems and needs of these children.

From an objective standpoint, these children show motor disturbances, and impairment of fine coordination, tremors, or choreoathetotic movements, changes in gait, difficulty in visual convergence and disturbances in associated arm movements and balance. As to social behavioral patterns, they have varying degrees of distractibility, shortness of attention span, hyperactivity, explosive aggressiveness, lack of spontaneous affectionate behavior, and varying degrees of emotional constriction with fearfulness, suspiciousness or persecution or its exact opposite in a form of fearlessness and lack of concern over possibility of physical injury.

PRESENT STUDY

An analysis was made of the cases of 16 children who had minimal brain damage. The age range was from seven to eleven years. Children with gross, neurologic defects or gross mental deficiency were not included. Detailed histories of birth and early development were taken, particularly in reference to illnesses or injuries which might be etiologic. In six cases there was a definite history of birth trauma, in two of premature delivery and in four of cerebral concussion. Two of the children had had febrile convulsions in infancy and one had had erythroblastosis fetalis. These patients were selected from a larger group of brain-damaged children on the basis of their having shown a clear and definite response to administration of drugs as judged both by clinical observation and the reports of parents and school teachers.

The complaints made by the parents and the observations of the school teachers showed pronounced consistency. Distractibility was an almost universal complaint, neither teachers nor parents being able to get the child to attend to a particular task for more than a few moments at a time. Almost continuous hyperactivity—running, jumping, climbing and destroying objects in an exploratory way—was frequently noted. Most of the children showed a wild, aggressive hostility which was aroused on slightest provocation and was directed toward parents, school and other children with equal frequency. A frequent complaint of both of the parents was that of emotional coldness so that praise or punishment seemed to have little restrictive effect.

Complete neurologic examination was done in all cases. In ten cases the results were essentially normal; in six, varying signs of mild impairment were noted, the most consistent being slight incoordination, clumsiness in gait and difficulty in carrying out fine coordinated movements. Choreoathetotic movements were observed with some frequency and could be best elicited by having the child stand with eyes closed and hands extended in front. Rotation of the body in its long axis on passive turning of the head was often noted, but not with the frequency of the foregoing neurologic signs.

Detailed psychologic testing was done in all cases and the results were of consistent pattern. There was a range of gross intelligence quotient from 76 to 110, with most of the children between 85 and 105. Pronounced difficulty with problems which called for concentration and span of attention was noted. On the Wechsler-Bellevue intelligence test there was a frequent and often pronounced discrepancy between verbal and nonverbal I.Q. evaluations, the nonverbal scores sometimes falling 20 to 30 points below the verbal. The implication was of weakness in areas requiring eye-hand coordination, spacial orientation, visual perception, analysis and search for details.

The Rorschach test showed many perseverations in precepts, with the child, once having offered a certain kind of interpretation, persisting in it whether or not the form was applicable to the ink blot. At times the children would recognize their response to the cards as being inaccurate or would even question why they continued to make such wrong interpretations. Color responses to the Rorschach test were often uncontrolled and pointed to the excitability and "formless" behavior which the child carried out in his every-day life.

As to results of the Bender-Gestalt test, which calls for visual perception and acuity, there was decided consistency among the children. The representations of geometric figures were distorted, figures were fragmented and there were pronounced perseverative tendencies. Disturbance in spacial orientation and visual relationships was also evident in a tendency to rotate figures.

While diagnostic reliance was placed primarily on the tests mentioned, having the patients make drawings of the human body frequently presented additional or confirmatory evidence of the disturbance in the integrative process of the central nervous system. The pictures showed grossly distorted precepts, with geometric figures, box-like bodies and distorted head, hands or facial features.

Electroencephalograms were made of all of the children studied, and in 11 cases the tracings showed definite disturbance in cerebral functioning. There was considerable variation in the electroencephalographic pattern but the most consistent finding was that of a diffuse dysrhythmia with a preponderance of slow wave activity and occasional spiking occurring in the temporal and frontal leads.

All the children were observed at play for whatever length of time was necessary in order to see a consistent and repeating pattern of functioning. Rather frequently during the first one or two periods of observation it was noted that the children would be somewhat inactive, showing little of the characteristic behavior the parents had described; but as soon as they were familiar with and more at ease in the situation, deviant types of behavior occurred with increasing frequency. Since the behavioral reaction of the children at play showed a continuous repeating pattern with inner consistency from child to child, a report of a typical period of observation for one of the children will be made:

In the waiting room, a nine-year-old boy was sitting beside his mother. The mother was looking at a magazine, rather anxiously attempting to get him to look at the pictures in order to avoid what

might be an embarrassing scene for her. On seeing me (Walker) he came bounding into the examining room, where he sat down in a chair and started to tell about the pet hamster that his parents had bought for him. But in the midst of this discussion his attention was drawn to the pencil and pad lying on my desk. He immediately dropped his remarks about the hamster which a few moments ago had been very interesting to him, and started to scribble on the pad. His movements had a quick and somewhat jerky quality. His attention then shifted to a set of plastic building-blocks and he started building a wall, as for a house. The wall leaned badly and, after several tiers of blocks were placed, it tumbled. The patient again began building the wall, again it fell. He did not recognize that the tilting of the wall was the reason for its collapse. After the third attempt, made in the same fashion and with the same outcome, he became flushed, obviously angry and knocked all the blocks to the floor, almost shouting that they were "no good." This general pattern of behavior was repeated through the period of observation—rapid shifting of attention and apparent difficulty in seeing the reasons for his failure in manipulation of mechanical objects. When he failed in these areas, his response was quick, impulsive, emotional and frequently indicating his feeling that the object that he was attempting to manipulate was at fault rather than his handling of it.

It is well accepted that the fundamental emotional needs of a child are affection, security, acceptance as an individual, a feeling of self-respect, achievement, recognition by peers, a feeling of independence, and ability to accept and live with authority. In a society such as ours where achievement forms a strong goal, the repeated failures of the brain-damaged child and the continuous frustrations to parents of seeing their children lag behind others in their own age group will strike strongly. The embarrassment over failure of the child as well as the genuine fear that the child might not be able to function satisfactorily as an adult, drives many parents into increasing their demands on the children, often enforcing these demands with punitive measures. While this serves as a means of releasing some of their feelings of frustration about the child, it is also done in part with the hope that increasing punishment will alter the child's behavior. Other parents when faced by their continuous inability to achieve certain goals for their children, will react by withdrawal and lack of emotional support.

We are sometimes too likely to think of a parent's relationship with a child as being an outgrowth of the parent's own inner psychic organization. The epigram, "There are no bad children, only bad parents," has been repeated often enough to focus attention on the parents' own underlying emotional problems as being a matter of great concern in treatment of a child with behavior problems. A neurotic person or one with a character disorder does not achieve an amelioration of symptoms simply by becoming a parent, and the symptoms of his own disorder will affect the child. However, a therapist must not become too engrossed in the parents' personality problems lest he underrate the effect of the child's behavior on the attitude of the parents.

During the preliminary period of study of the children in the present series, the parents were seen in a series of interviews by a psychiatric social worker. An assessment was made of the parents' attitudes towards the children, particularly in terms of the parents' understanding of the needs and problems of the child and of their feelings of acceptance and warmth. In only one instance did the parents have a genuine feeling of warmth and affection. The parents of two of the children overprotected them, over-restricted their activity and treated them as infants. Two other children were being reared in an environment of open hostility on the part of the parents. The parents of the remaining 11 children showed fluctuations between attitudes of rejection and efforts to isolate themselves from the children and the problems which their behavior produced.

During the interviews the primary topics brought up for discussion by the parents centered around the parents' feelings of annoyance or frustration, and very little time was given to consideration of the child, his feelings and his needs. Two weeks after the beginning of a chemotherapeutic regimen which brought about decided improvement in the behavior of the children, a great change was noted in the attitudes of the parents of 11 of the 16 children.

At this time there was a sudden increase of remarks indicating an interest in the children, an awareness of their problems and a sympathetic understanding of their difficulties. Concomitantly, there was a notable decrease in expression of opinions that the child's behavior was mean, willful, or purposefully used to embarrass or punish the parent. As to the parents who showed little change in attitude following the improvement of their child, two had psychoneurotic symptoms so severe that individual psychotherapy had been recommended for them. The parents of two other children were under so much pressure from pecuniary difficulties and physical illness that it was very hard for them to turn their attention away from their own pressing problems to the problems of the child.

Although parental attitude toward the children changed to some degree during the preliminary periods in which they were given an understanding of the organic brain syndrome and the particular

problems of the child, the maximum change in attitude toward the children followed the children's change in behavior.

No attempt was made to make careful evaluation of differences in the effectiveness of various drugs used in the present study. Various drugs, including Dilantin® (diphenyl hydantoin), amphetamine, Benadryl® (diphenhydramine), phenobarbital, reserpine and chlorpromazine, were used. Excepting two children who showed a better response to chlorpromazine, Dilantin® seemed to bring about the greatest benefit. The observations as to Dilantin were similar to those reported by Walker and Kirkpatrick[6] in 1947. In several of the cases some further improvement occurred when amphetamine was given additionally, but this was not a consistent finding. At no time was a sufficient amount of any of the drugs used to cause daytime drowsiness. The primary changes noted after administration of drugs was started were a decrease in distractibility and hyperactivity and a decrease in sudden and violent, emotional outbursts.

The reactions of the parents to their own feelings of frustration over the symptoms of the brain-damaged child creates an environment in which the child is under continuous stress because of lack of acceptance by the family group. With regard to rejection, Bender[2] observed that in home settings in which the needs of the brain-damaged child are met, the damage-and-rejection syndrome does not develop in its entirety. While ordinarily the organic damage is not reversible, the manner in which the child develops reaction patterns directed toward his environment will be largely dependent upon the acceptance and support which he receives from the parents, school personnel, siblings and peers.

The increasing acceptance of a brain-damaged child by the parents enables them to give greater support, and to permit greater dependency when it is needed, without feeling that they are interfering with the child's progress; and it also permits them to continue this support until the child seeks emancipation from the overprotective environment. Praise and encouragement can be more freely given on the basis of the child's efforts and accomplishments without reference to what other children in the same age group are accomplishing.

While it is evident that the diagnosis of the organic brain syndrome in children with behavior disorders relieves many of the parents' feelings of guilt and would seem to permit them to shift responsibility for their children's behavior from themselves, at the same time it should be noted that as the children improve, the parents were willing to do more, to give more and to assume a closer relationship.

It was noted in the present study that while their better understanding of the symptomatology of the organic brain syndrome increased the parents' ability to create an environment conducive to feelings of security rather than of frustration for the child, behavior of the child himself seemed to play a large part in attaining these goals.

2007 Wilshire Boulevard, Los Angeles 57 (Walker).

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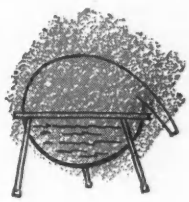

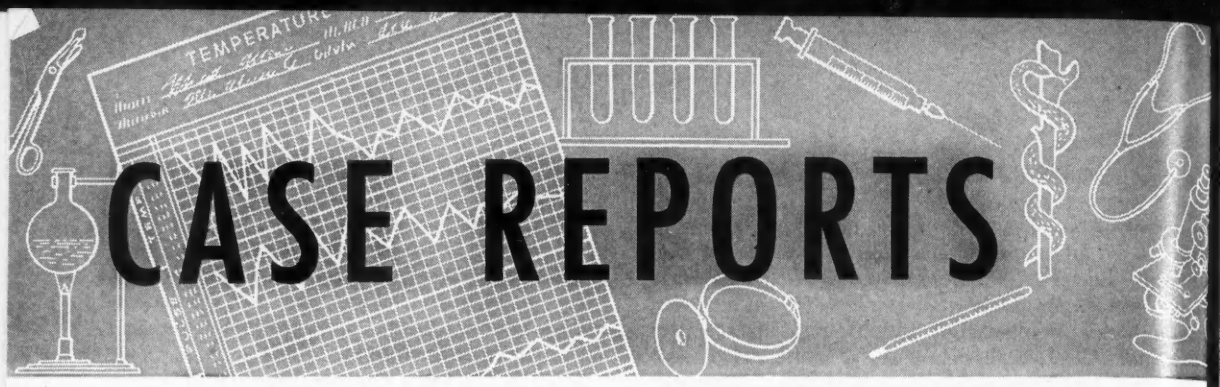

Gangrene of the Thigh Owing to Venous Occlusion

N. S. LOVELL, *M.D.*, and
E. G. CLAUSEN, *M.D.*, Oakland

GANGRENE caused by venous occlusion is rare. There have been no reports in the medical literature of gangrene occurring in the thigh alone; gangrene of this kind is preceded by "blue leg," or phlegmasia caerulia dolens. In about one-half of all reported cases of venous occlusion gangrene, amputation was required; and the mortality rate for all reported cases was about 25 per cent. The purpose of this report is to call attention to this unusual condition in which prompt treatment may avert tragic consequences.

REPORT OF A CASE

A 38-year-old Caucasian woman in her first pregnancy had cesarean section because of fetal-pelvic disproportion. The postoperative course was uneventful except for wound infection. Ambulation was started on the first postoperative day. Fourteen days after operation, the patient noted bluish discoloration and pain in the left thigh. As the day progressed the entire leg became quite blue. Edema of the thigh appeared first, followed in 24 hours by involvement of the entire leg. The involved extremity was slightly warmer than the other leg and peripheral vessels were normal. During the next four days the left foot and leg became more edematous and the bluish discoloration decreased. During this four-day period the extremity was elevated and Dicumarol (dicoumarin) was given in doses of 300 mg., 200 mg. and 150 mg. on successive days.

At 2 o'clock in the morning of March 29, the fifth day after discoloration had appeared, the patient was awakened by pain in the side of the left thigh. At the site of pain there was an oval area of discoloration which enlarged to diameters of 24 x 10 cm. This was ascribed at the time to a bleeding tendency, and on March 30, 1957, Dicumarol was discontinued and 50 mg.. of Mephyton® (vitamin K_1) was given intravenously. The clotting mechanism, as determined by platelet content and by bleeding and clotting time, was normal. Chymotrypsin

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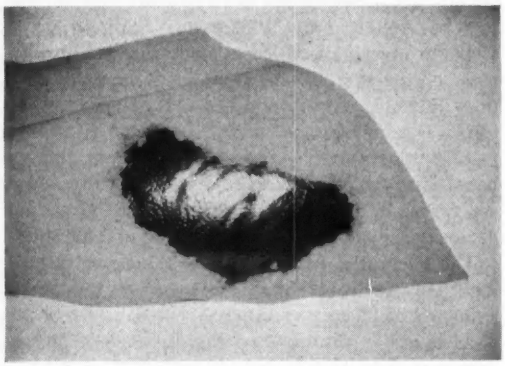

Figure 1.—Gangrene of the thigh owing to venous thrombi.

was given intramuscularly, 0.5 cc. every eight hours for 11 days. Approximately five days after the onset of discoloration a black bulla appeared over the surface. Resolution of the bulla left an area of hard gangrene about 16 x 8 cm. (Figure 1). The patient's temperature rose to 100.6°F. The day before gangrene appeared, the prothrombin time was only 69 per cent of normal.

On April 9 the area of dry gangrene was excised. The subcutaneous tissue was much more extensively involved than the skin, the fat obviously necrotic and infiltrated with blood. The tissue was removed down to the tensor fascia lata, where the pathologic process ended. Upon examination of the tissues, complete thrombosis of all venous channels was noted. The arteries were intact without evidence of thrombosis. A portion of the operative site was closed primarily and the remainder with a split thickness graft. Four hundred thousand units of procaine penicillin was given intramuscularly every 12 hours for ten days. The area healed without complication.

DISCUSSION

Phlegmasia caerulia dolens, or "blue leg," is infrequently associated with phlegmasia alba dolens and is thought to be due to almost complete obstruction of the venous return. In reported cases, varying patterns of development were noted. In some instances the first sign of phlebitis was the appearance

of a "blue leg," as in the present case. However, the most common pattern was the appearance of a "blue leg" superimposed on active phlebitis. The condition is associated with a great deal of pain and swelling. The lower leg is involved most frequently, although in 20 per cent of the cases reported the upper extremity was involved. In some instances the peripheral pulses were absent and there was early onset of gangrene, often thought at first to be owing to arterial occlusion. However, supported by studies of removed tissue, most authorities agree that the gangrene in these circumstances is due entirely to complete venous blocking, the arteries remaining intact. The area of involvement is primarily superficial tissues. The possibility that gangrene may complicate "blue leg" makes energetic therapy mandatory.

With complete thrombosis of the venous system, the arterial system functioning normally, the following physiologic changes occur: Arterial blood enters the affected area at normal arterial pressure but, due to venous obstruction, stagnation and hypoxia is progressive. Subsequently the noncolloidal and then colloidal elements extravasate, edema and discoloration resulting.

The use of anticoagulants in the treatment of this condition is universally approved. In cases in which blue discoloration of the extremity is the first sign of phlebitis, heparin should be administered until the prothrombin time is brought down to therapeutic levels by the use of thromboplastin depressant drugs. The use of paravertebral block has proved to be of doubtful value.

In addition to the usual methods of treatment for phlebitis, Veal[3] suggested the use of passive muscular exercises to prevent gangrene. The exercise he described was to elevate the involved extremity to 60 or 70 degrees, then rapidly extend and flex the foot and thigh in the hope that blood will be massaged through the venous system until the collateral vessels have had opportunity to develop. These exercises are done at short intervals until cyanosis disappears.

DeBakey[1] reported two instances in which patients were operated upon and a clot removed from the femoral vein. He expressed belief that this had prevented gangrene of the extremity. There have been no further reports on the use of this method.

Fisher and Wilensky,[2] reporting upon the use of trypsin parenterally for acute and chronic thrombophlebitis, noted accelerated subsidence of pain, heat, tenderness, edema, erythema, streaking leukocytosis and Homen's sign if present. Acceleration of the sedimentation rate subsided within two or three days. They postulated that the enzyme dissolves the thrombi. Various investigators, reporting on experiments with dogs, suggested that trypsin brings about increased size of lumen in thrombosed veins, but other observers were unable to confirm the occurrence. It is generally agreed that acute thrombophlebitis of less than three weeks duration responds more satisfactorily to trypsin therapy.

SUMMARY

A case of gangrene of the thigh, of venous origin, is presented. Recognition of serious implications of "blue leg" with prompt therapy may avert partial or total loss of the extremity.

418 Thirtieth Street, Oakland 9 (Clausen).

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Paroxysmal Ventricular Tachycardia

A Case Study

JUDD MARMOR, *M.D.*, and MORLEY J. KERT, *M.D.*, Los Angeles

THAT EMOTIONAL STRESS is often a relevant factor in the etiology of certain kinds of cardiac arrhythmia has been ably documented by numerous observers[1,2,4,5,6,8] and is now widely recognized. Extrasystoles, sinus tachycardia, paroxysmal auricular tachycardia and paroxysmal auricular fibrillation have all been shown in certain instances to be significantly related to psychic stress situations, not only cases in which there is pathologic change in the heart but also when the heart is entirely normal structurally so far as can be determined by any test now in use.

The term, *emotional stress*, is rather broad and often loosely used. What constitutes stress for one person may have no such effect on another. Similarly, the terms *anxiety*, *hostility*, and *tension* are often used in a rather general way to describe psychic reactions which deserve more precise formulation.

The following case report is presented with the conviction that the specific psychodynamic factors described not only shed light on the genesis of cardiac arrhythmia in this particular patient but also have more general implications. The cardiac arrhythmia, in this instance, moreover, was of special interest because it was of a relatively rare kind—paroxysmal ventricular tachycardia, a condition usually assumed to be associated with severe organic

From the Departments of Psychiatry (Marmor) and Medicine (Kert) of the School of Medicine, University of California at Los Angeles, Los Angeles 24.

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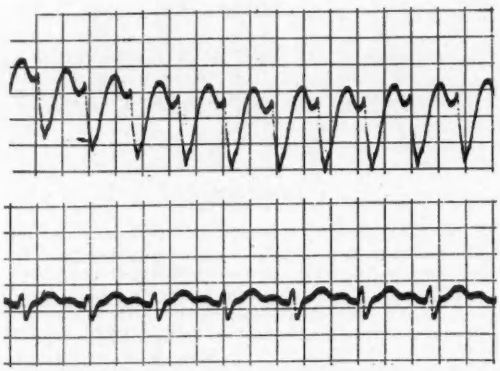

Figure 1.—At top, lead 1 in electrocardiogram showing ventricular tachycardia. Below, six hours after administration of quinidine and procaine amide hydrochloride, the rate was down to 150.

heart disease and recent myocardial infarction, and one in which, so far as the authors have been able to determine, psychological factors have not been considered particularly relevant.*

The patient, a tall, handsome man in his middle forties, was referred by a cardiologist with the following clinical history:

Eighteen months before consulting the cardiologist the patient, while leaning over to wash his face, became aware that his heart was racing at a rate which he calculated, from his pulse, at 300 a minute. A physician was called and he was treated with vagal stimuli without effect, and then was given quinidine which apparently stopped the attack in about four hours. An electrocardiogram made 13 days later was said to be within normal limits. Several months later, the patient had another attack, was taken to a hospital where the heart rate was found to be 280, and an electrocardiogram identified the rhythm as ventricular tachycardia (Figure 1). He was given quinidine and Pronestyl (procaine amide hydrochloride) and at the end of six hours the rate was down to 150. Seven weeks later he had another attack which was treated with quinidine given intravenously. The patient then was given 2.3 gm. of quinidine a day by mouth, but he continued to have attacks with gradually increasing frequency. It was at this point that he was referred to the cardiologist.

When seen by the cardiologist, results of physical and laboratory examinations were all within normal limits. The pulse rate was 66, the volume good and the rhythm regular. The blood pressure was 120/80 mm. of mercury. Heart tones were of good quality. There was a grade I, pulmonary systolic murmur. P_2 was louder than A_2. The heart was normal in size in all fluoroscopic views and the aorta appeared normal. Lung fields were clear. Peripheral pulses in the lower extremities were of good quality. X-ray films of the chest confirmed the fluoroscopic observations, and the total transverse diameter of the heart was observed to be 152 mm., well within the normal range for the patient's age and height. An electrocardiogram, including standard unipolar limb and unipolar chest leads, showed a tendency to low voltage in standard and limb leads and a QRS complex interval which was at the upper limits of normal. The cardiologist did not consider the electrocardiogram, in its entirety, to be outside normal limits, although he noted that some electrocardiographers might have interpreted it as showing intraventricular block.

Since the history strongly suggested that each of the episodes of tachycardia had been preceded by some emotional incident, it was recommended that the patient have psychiatric consultation. He was resistant to this suggestion, however, and instead sought another cardiological consultation in a different city. There he was given two gm. of Pronestyl and 40 minims of tincture of belladonna five times daily. Despite these heroic doses, he continued to have episodes of ventricular tachycardia which frequently required intravenous injection of Pronestyl for control. The patient then finally agreed, albeit reluctantly, to have psychiatric consultation, and then to undertake psychotherapy.

The following history gradually emerged in the course of psychiatric interviews. His parents were intensely religious, middle-western people. The father was a stern and harsh disciplinarian who frequently employed corporal punishment. The mother, a relatively weak and passive person, played a secondary role in the household, and was little source either of affection or emotional security to the patient. As a result, he grew up feeling contempt for her weakness, an attitude which he subsequently transferred to most other women. He always felt closer to his father, whose strength and power he admired even though he feared and resented it also.

His childhood and adolescent years were characterized by an attitude of intense rebelliousness against all the authority symbols in his life. He was a disciplinary problem at school and was in constant conflict with his father at home. At the age of 15, he ran away from home. When hunger forced him to return a week later, his father beat him unmercifully, but then permitted him to drop out of school and go to work. After a number of menial jobs, in which he was extremely unhappy, he secured work in an engineering firm. Engineering projects had interested him as far back as he could remember, and he took to the work with avidity. He worked at it with enormous energy and showed such natural talent for it that within four years, and at the age of only 21, he worked his way up to a position of top responsibility within the firm and was receiving a very high salary. A year later, when his employer became ill, he was entrusted with the management of the entire firm. He acquitted himself so well in this position that in two years he more than doubled the business of the firm. Meanwhile he was married, set

*Dr. Louis Katz in a discussion of a paper by Romano and Engel (Psychosom. Med., 7:12, 1945) mentioned having seen "one or two [cases] of reversible ventricular *fibrillation*, in which the attacks could be induced by an emotional upset."

up an expensive home and spent money with a lavish hand.

With the economic crisis of 1929, however, the firm collapsed, his savings were wiped out on the stock market, and he was left penniless. For the next eight years he worked with great energy building up an independent engineering practice. Although it was a long struggle, he gradually began to achieve greater and greater recognition, and finally emerged as one of the outstanding engineers in his community. He always felt extremely insecure professionally, however, due to his lack of a formal academic training in his field, even though he had mastered through practical experience and individual study all the knowledge and techniques which he could have obtained at an engineering college.

During the first years of his marriage, his sex life and relationship with his wife were excellent, but after the birth of their only child, his wife developed strong fears of pregnancy and began to withdraw sexually. From that time on the patient began to have extra-marital relationships which increased in frequency and intensity, so that he began to acquire a reputation as one of the Don Juans of his community. All of this, however, went on without the wife's conscious knowledge, but with a constant fear in the patient's mind that sooner or later his infidelities would be exposed to her.

Hand in hand with this sexual promiscuity went tendencies to "cut corners" in his professional practice and to take dangerous and unnecessary risks. His first attack of tachycardia occurred during a period of great personal and professional tension when he became involved one afternoon in an affair in his own home with a domestic servant. This was the first time he had ever done this. In the midst of the sexual relationship he was suddenly overcome with an awareness of the enormity of the risk that he was taking. His wife might return at any moment, and there were other people working around the house in a way that made discovery not unlikely. He had a sudden onrush of tremendous anxiety, and simultaneously extremely rapid tachycardia developed. He was convinced that he was having a fatal heart attack and called his physician. An injection of quinidine finally stopped the attack, but only after four agonizing hours.

The second attack, several months later, began during an episode in which there was an imminent danger of his being exposed and humiliated for an unwarranted business risk which he had taken.

During the two years that followed before his beginning psychotherapy, these same factors in his personal and professional life kept him in a state of persistent apprehension. His love life had become so complicated as a result of his pyramiding affairs that the danger of exposure constantly grew greater. The letters, phone calls and importunings of his various girl friends, old and new, were becoming increasingly difficult to handle. At the same time, pressing and important business problems were coming to a climactic focus. He was like a juggler who had taken on more than he could handle and who was now trying desperately to avoid the one tiny slip that would inevitably bring the entire unstable dynamism crashing at his feet. Throughout this period he suffered from recurrent anxiety dreams which centered symbolically around two main themes: (1) of feeling hopelessly trapped, and (2) of being in danger of being castrated.

In the course of therapy, other facts of interest emerged. His earliest memory, going back to his fourth year, was of looking at a distant hill outside his bedroom window, and thinking that if only he could climb to the top of it he could touch the sky. Several years later he did climb the hill only to find that "the sky was over the next one." He recalled his intense disappointment, but also his determination to keep climbing the hills until he got high enough to touch the sky.

From adolescence on, his great secret ambition was to be a bull fighter, and watching bull fights was always an enormous source of excitement to him. At the age of 17 he had a brief fling at prize fighting. After a series of successes in a number of preliminary fights, he over-ambitiously sought out a match with a much more experienced fighter and received so humiliating a beating that he retired from the ring permanently. However, throughout his adult years he continued to show a strong predisposition to settle differences of opinion with people by physical violence. He would do things of which he was tremendously afraid just to prove to others that he wasn't really frightened. To appear ridiculous in the eyes of others was the most traumatic experience of which he could conceive. Although painfully aware of many personal and professional inadequacies, he felt it of paramount importance that no one else must ever know of them, and concealed his apprehension with an air of bravado. Once he made a decision he was rigidly stubborn about maintaining it, and would never admit an error. He had no intimate friends and, before therapy, had never confided in anyone, even his wife.

He was a lavish spender and a generous tipper. He preferred to give rather than to receive. Giving made him feel strong and manly. Receiving made him feel weak, inadequate and obligated. In his professional work he showed great esthetic sensitivity as well as originality. He was constantly seeking to devise new techniques and trying "to climb to new heights." He had a strong need to become known as the biggest and best engineer of his kind in the United States.

Several months after the beginning of therapy, an incident occurred which not only had important psychological significance but also led the cardiologist to revise his opinion concerning the patient's cardiac status. On a vacation week-end the patient challenged his only son, a tall, husky, strapping youngster of 19, to a long swimming race, determined to "show the boy that he was still the boss man." He managed to win, but only by dint of almost superhuman exertion at the finish, and he

fell exhausted on the beach. Although he had no attack of ventricular tachycardia, he felt upset at his exhaustion and sought another cardiac examination. At this time an electrocardiogram showed abnormal T waves in V_5 and V_6 which the cardiologist felt were indicative of "anterolateral myocardial changes, probably on the basis of coronary artery disease."

The patient was treated by a psychoanalytically-oriented face-to-face psychotherapy for ten months —three times a week for the first six months, and twice a week thereafter. This form of therapy was necessitated by the patient's enormous resistance to a more intensive analytic approach. Although he rationalized this resistance mainly on financial and temporal grounds, there was no genuine basis in reality for these excuses. It was clear that his resistance had deeper origins, centering around his inability to tolerate a situation in which he would have appeared in his own eyes to be passively submissive and not in control.

Despite this limited approach, the patient was able after the first three months of therapy gradually to reduce the amounts and finally to stop taking quinidine, belladonna and Pronestyl. He had no further attacks of paroxysmal tachycardia thereafter, notwithstanding several extremely trying periods in his personal and professional life. Once the symptoms which had brought him into therapy had ceased, however, the patient's resistance to a more thoroughgoing working-through of his characterological problems increased, and against advice he insisted upon terminating therapy.

Fourteen months later, when the patient had been free from attacks of tachycardia for 21 months, a tragic postscript had to be added to his case report. Late one Friday afternoon, the patient and his wife went out to look over one of his engineering projects, which was in process. He became highly annoyed at discovering that his workmen had failed to move a large boulder to the top of a hill as he had requested. In spite of his wife's fervent remonstrations that it was a task for at least two men, he insisted on trying to move the boulder up the hill by himself, then and there. Straining and tugging, red in the face, he succeeded in rolling it two-thirds of the way up, when he suddenly collapsed and died instantly. Postmortem revealed, not a coronary thrombosis, but acute myocardial failure with moderate coronary arteriosclerosis.

Thus the manner of his death, like the pattern of his life, reflected with a kind of fateful inevitability the dynamics of his personality structure—the compulsive need to prove his masculinity and to counterphobically deny his underlying passivity, inadequacy feelings and fears. He died as he had lived, straining to the very end to climb to the top of the hill—the hill of phallic exhibitionism.

It is impossible to draw any general conclusions from a single case. The evidence strongly suggests, however, that this patient's tendency to reactively deny the existence of fear, coupled with his compulsive need to court danger, was a significant determinant in the cardiac episodes. Tachycardia is the heart's characteristic way of responding both to anger and to fear. Where these emotions are accompanied by appropriate activity the tachycardia is physiological and is not subjectively perceived. When, however, the activity is inhibited, the tachycardia is perceived as a subjectively unpleasant sensation.

It is not intended to imply from this, however, that similar patterns must be operative in all cases of tachycardia in which emotional factors are implicated. On the contrary, available evidence suggests that it is not only possible, but highly probable, that in other kinds of personalities repressed rage, rather than repressed fear, can be the significant triggering mechanism. Duncan and co-workers, Katz and co-workers[4] and Master and Eichert[6] described a number of such cases, although also confirming the importance of repressed anxiety in other cases.

It is not within the purview of this communication to theorize about the physiologic mechanism of such arrhythmia. It may be pertinent, however, to mention the studies of Stevenson, Duncan and Wolff,[8] who demonstrated that cardiac output may be increased by emotional states such as anxiety or resentment much more than by the maximal exertions of everyday life, such as climbing stairs; and also the findings of Levy, White and others[5] that persons with pronounced tachycardia show an increased liability to the later development of structural heart disease. This would suggest that the cardiac adaptational demands of prolonged emotional stress may be important in the etiology of structural heart disease. Also it underlines the importance of exploring the emotional factor in all cases of paroxysmal arrhythmia, and of treating it whenever it is found to be present. The case here presented illustrates the fact that emotional stress may be an etiologic factor in paroxysmal tachycardia—even in the presence of structural heart disease. That the structural heart disease in and of itself was not a sufficient explanation for the patient's attacks is indicated by the abatement of attacks under psychotherapy, although they had stubbornly persisted for almost two years before psychotherapy.

The question of why this patient had a ventricular tachycardia instead of the more common auricular variety is one that cannot be answered with certainty. One is forced to assume the presence of an irritable ventricular focus based on myocardial damage secondary to coronary artery disease. Under the influence of the humoral and autonomic changes which accompanied intense and prolonged anxiety, this ectopic focus evidently took over the role of pacemaker.

SUMMARY

A case of paroxysmal ventricular tachycardia in which emotional stress appears to have been the precipitating factor is presented. The relevance of the

patient's underlying character structure—his compulsive need to prove his masculinity, and his counterphobic need to deny his underlying passivity, fears and inadequacy feelings—is discussed.

420 North Camden Drive, Beverly Hills (Marmor).

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Philodendron Dermatitis

CLETE DORSEY, *M.D.*, Pasadena

PHILODENDRON or *Scandens Cardatum* (Figure 1), is a vine-like, tropical plant that has become popular for growing in a pot inside houses.

Recently I observed a case of dermatitis caused by this plant.

REPORT OF A CASE

A 23-year-old Mexican girl was seen one week after the onset of a moderately severe dermatitis of the arms, face and neck. A papulovesicular eruption was present on the dorsa of both hands, the inner wrists, the inner forearms and the outer surfaces of both upper arms. The skin of the eyelids, face and neck was diffusely swollen and erythematous. Itching was severe enough to prevent sleep. The eruption was similar to that of a mild reaction to poison oak.

The patient immediately suggested that the dermatitis might have been caused by Philodendron plants with which she came in contact in her daily work in a commercial greenhouse. She had been told there that Philodendron plants were toxic to the skin. To investigate this possibility, dermal patch tests were done with leaves and stems of all of the plants encountered in her work. The results of all tests at the end of 24 hours were negative. Because it had dried, the Philodendron patch test material (crushed leaves and stems) was moistened with water. At the end of 48 hours, the tests were examined again. There was no reaction to any of the other materials, but there was papulovesicular dermatitis (Figure 2) at the site of the Philodendron patch.

The original dermatitis cleared in two weeks on therapy which included wet dressings, application of an ointment containing hydrocortisone and terramycin (Terra-cortril®) and injection of corticotropin gel subcutaneously. The patient gave no history of a previous allergic reaction. The present attack came on two weeks after she had begun planting Philodendron cuttings.

Three other persons worked at the nursery at

Figure 1.—A typical small Philodendron plant. The color is a uniform bottle-green in both the leaves and stems.

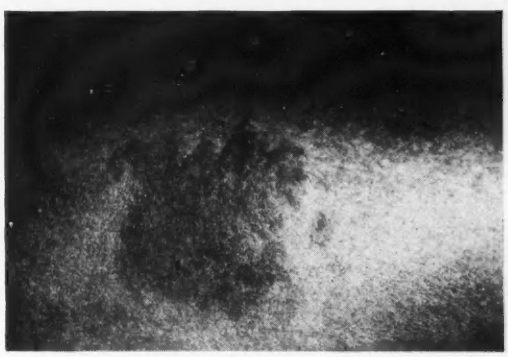


Figure 2.—Patch test reaction to Philodendron leaves and stems (crushed and moistened with water). This photograph was taken four days after the patch was applied. The reaction occurred at about 36 hours after application of the test.

From the Department of Dermatology, University of Southern California School of Medicine, Los Angeles.

Submitted November 27, 1957.

which the patient was employed—the owner, his wife and a Mexican gardener. The owner's wife was so sensitive to Philodendron that she had given up working with the plants. The owner also had allergic sensitivity to these plants but had become "hardened" and now had only mild, transient dermatitis when he worked with them for long periods. He said that a number of other workers in previous years had had to leave because of sensitivity to Philodendron; and he had found that Mexican workers were rarely affected.

DISCUSSION

I could find only one other report of a case of Philodendron dermatitis in the literature. Harris[1] in 1942 described chronic dermatitis of the eyelids in a 23-year-old housewife which was traced to Philodendron plants in her home. The lapse of 15 years between Harris' report and this one would suggest that Philodendron dermatitis is extremely uncommon. Yet such is not the case. Six commercial nursery owners were interviewed. Two of them reported a high incidence of Philodendron sensitivity among their workers. Occasionally the disease was so severe the employee had to avoid exposure to the plant, but in the larger proportion of cases it was relatively mild. Four nurseries reported that none of their employees had ever had allergic reaction to Philodendron. This difference could not be explained except perhaps by the fact that these four dealt relatively little in Philodendron. Nurseries where dermatitis had occurred reported that the plants were more troublesome when the leaves were wet. It is noteworthy in this regard that the woman in the present case did not show a positive reaction to a patch test until the test material was moistened with water. Also, the patient in the case reported by Harris washed the leaves of her plants now and then to keep them glossy and the dermatitis always became worse soon afterward. These observations would suggest that the toxic principle of Philodendron is water-soluble and that it does not lie on the surface of the leaves but within them.

A paradox in Philodendron dermatitis is that it occurs frequently in workers in commercial nurseries, yet apparently almost never in housewives who cultivate the plants at home. Possibly many cases in housewives are not diagnosed. However, I believe that the explanation lies in the difference between the way this plant is cultivated in nurseries and in the home. Plants grown in the home are rarely touched, but in a nursery a worker may come in contact with cut leaves and stems hundreds of times a day. Furthermore, in the home plants are watered cautiously, usually at the base to avoid dripping and splattering, but in a nursery they are watered in such a way that the entire plant becomes wet. It is conceivable that different methods of watering used in different nurseries may account for differences in the extent to which dermatitis occurs among workers.

SUMMARY

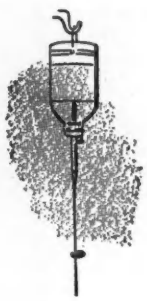
Contact dermatitis from Philodendron (*Scandens Cardatum*), a very popular house plant, occurred in a woman who handled the plants in a commercial nursery. A previous investigator reported a case in a woman who cultivated and cared for one of the plants in her home.

Apparently this disease is not uncommon in workers who cultivate Philodendron commercially. Whether or not it is common in housewives who cultivate it at home is not known.

65 North Madison Avenue, Pasadena.

REFERENCE

1. Harris, J. H.: Dermatitis of the eyelids due to Philodendron (Scandens Cardatum) plants, Arch. Dermat. & Syph., 45: 1066, June 1942.



California MEDICINE

For information on preparation of manuscript, see advertising page 2

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EDITORIAL

United Funds and Voluntary Health Agencies

THE PAST FEW YEARS have witnessed the development of an increasing controversy between the United Funds and the Voluntary Health Agencies. At times the dispute has descended to levels neither mature nor dignified.

The genesis of the controversy is simple. United Funds have been created to put an end to multiple fund drives for worthy causes. The argument that one might contribute once—and be done with it—appears attractive, particularly to those whose knowledge of the functions of the organizations involved is limited.

These organizations fall into two principal categories. One group consists of local welfare agencies. The other is composed of national health agencies, among which are such highly respected bodies as the American Cancer Society, the American Heart Association, the National Tuberculosis Association and the National Foundation for Infantile Paralysis. These have contributed significantly to the health and medical welfare of the American people. All have state and local subdivisions.

It is worth while to examine the functions of the two groups of agencies. Both are devoted to meeting human needs and are therefore admirable. They have certain points of similarity but greater differences.

The local welfare organizations were established to care for the needy in their own communities. The needs of one community may vary from those of another and may include providing employment, food, shelter, clothing, transportation, medical and hospital care, recreation facilities and other services.

It may be laudable for a community group to survey the overall requirements for these strictly local services, to raise funds in appropriate amount and to distribute them on the basis of a generally acceptable formula. No valid objection to this procedure can be offered, and local welfare organizations wishing to become a part of United Funds should be free to do so.

The value of a particular local organization must be estimated at the community level. Worthy welfare programs deserve our support and when they are joined together in a common campaign for funds we should assist in the project.

The situation with the Voluntary Health Agencies is quite different. The primary purposes of these agencies are to support research, to conduct programs of public education and to assist in professional education. The service aspects of most agencies are limited and constitute a minor portion of their activities. The principal exception is the National Foundation for Infantile Paralysis. As important, however, as the service program of the Foundation may be, it pales into insignificance when compared with the research which led to the development of the Salk vaccine.

The reduction of the death rate of tuberculosis can be attributed in part to the efforts of the Tuberculosis Association. It becomes progressively more apparent that the conquest of cancer and cardiovascular diseases will be accomplished through research into the causes of these conditions and into improved methods of prevention and treatment. Progress is being made in these fields, but much more remains to be done.

It is not easy to decide which research projects deserve support, even at the national level, where maximum information and the services of experts are available. This is much more difficult to accomplish at the state level and it is virtually impossible to do so realistically in the local community. National leadership is essential.

Public education is a prime function of the Voluntary Health Agencies and is particularly important in the field of cancer. The annual crusade of the American Cancer Society in April does more to inform the public of the necessity of early diagnosis and early effective treatment than the year around educational activities of the Society. Thousands of dedicated volunteer workers disseminate important information about cancer while soliciting contributions. The solicitation of funds and the education of the public are inextricably linked.

The individual Voluntary Health Agency must be judged on the basis of its announced objectives, the effectiveness and fidelity it displays in pursuing those objectives and the soundness of its budget. A reasonable overhead and economy of operation are important items.

In some communities great pressure has been exerted upon local branches of the Health Agencies to force them into United Funds. Coercive tactics, misrepresentation and subterfuge have been used. In certain instances medical societies have been induced to set up local research foundations which they are ill equipped, from the standpoint of special skills, experience and facilities, to administer wisely.

This mechanism has been used to enable United Funds to receive donations in the names of diseases the Voluntary Health Agencies were founded to combat. The freedom of the agencies to conduct their own campaigns has been curtailed.

Where long-time arrangements have existed between United Funds and Health Agencies involving participation of the Agencies in campaigns of the United Funds, the experience usually has been unsatisfactory. Smaller sums have been raised for specific purposes than could have been achieved by the agencies alone. It must be recognized that local service demands tend to take precedence over broader programs. The end result has been less well financed research and injury to the public education endeavor.

At the recent hearings of the Shipman Committee in Chicago, it was convincingly demonstrated that the United Community Funds and Councils of America (the national organization of United Funds) is determined to eliminate the fund-raising activities of the Voluntary Health Agencies. It was further developed that donations designated for specific purposes will be accepted by United Funds temporarily, but ultimately the donor probably will be deprived of the right to have his gift allocated according to his desires.

We commend the Voluntary Health Agencies for their refusal to accept money from the United Funds and for directing their state and local units to do likewise. Should the efforts of the United Funds and Councils succeed, the destruction of the Voluntary Health Agencies will be inevitable. These agencies have a record of accomplishment and are rendering constructive service to the American people. Their loss would be a catastrophe.

We, as members of the medical profession, recognize the value of the Voluntary Health Agencies. We also dislike and resent coercion—whether it be by government or by others who arrogate decision as to the course we should follow.

To remain effective, the Voluntary Health Agencies must maintain their independence and retain their identities. It is vital that they not be dominated by other influences or be submerged in larger organizations.

The medical profession probably represents the most potent body of informed public opinion in this controversy. We are convinced that the Voluntary Health Agencies are performing a valuable service. We must not permit ourselves to be coerced or cajoled into programs designed to destroy them. The loss of these bodies would be an open invitation to government to step into the void thus created. Governmental agencies have a place in the financing of research, but to surrender the field to them completely would be to court disaster.

1958 Annual Session

CALIFORNIA MEDICAL ASSOCIATION'S 1958 Annual Session will again be held at the Ambassador Hotel from the 27th to the 30th of this month.

Lest you think the location of the meeting has got stuck in a rut, please remember that this year the meeting was to have been held in San Francisco; the change to Los Angeles was made when the American Medical Association scheduled its 1958 meeting for San Francisco, an event calculated to drain interest away from a C.M.A. session in the same city just a month earlier.

One pronounced change in the scientific program this year will be three postgraduate courses for which official credit will be given by general practice organizations. Each of the three Los Angeles medical schools will supply the program and faculty for a postgraduate course. To help pay the cost of these courses and to qualify them for credits by organizations who give credits to members for postgraduate work, a fee of $25.00 is to be charged for each.

On Sunday afternoon and Monday and Tuesday mornings, the University of Southern California medical school will stage a course on liver diseases, one session to be held at the Los Angeles County General Hospital.

University of California at Los Angeles will put on a course on the management of trauma on Monday, Tuesday and Wednesday mornings.

On the same mornings the College of Medical Evangelists will devote nine hours to a course on abdominal pain.

The usual business and scientific meetings will again be held. The technical and scientific exhibits always so popular at medical meetings will occupy an important place on the program and will again be housed in the handsome exhibit rooms rebuilt with great care by the hotel just two years ago.

Guest speakers will appear before the general meetings, section meetings and postgraduate courses, each participating from his own specialty angle.

For the benefit of Los Angeles physicians who enjoy Wednesday afternoons away from their offices, the exhibits will remain open through the greater part of that afternoon. For those too busy to come to the meeting earlier, this presents a chance to see at least a part of the show.

A complete program for this session appeared in CALIFORNIA MEDICINE last month. If you haven't yet examined it, there is still time to pick out your own areas of interest and arrange to take part.

Letters to the Editor . . .

February 17, 1958

To the Editor:

MANY PHYSICIANS are growing mindful of a dilemma in philanthropic giving that is particularly important to members of the medical profession. Federated funds have been organized in many communities throughout California to collect and apportion public contributions for the many health and welfare services that are an integral part of our community life. And federated fund-raising has proved, in many instances, an efficient and equitable means of providing support for these local agencies. On the other hand, certain large national research-oriented health agencies have found that independent fund raising, combined with a public education campaign, is necessary to meet national needs of medical investigation and ancillary service in their respective fields.

As a giver, the physician may find that giving once to the full extent of his ability to some united type of fund is a convenient way of meeting his philanthropic obligations. But, as a physician, he is well aware of the creative work done by certain health agencies in research and community service, and should feel a special professional responsibility for the welfare and continuing growth of these agencies.

The dilemma has been sharpened by the effort of many local federated fund organizations to include national health agencies in their "one big give" appeal. Medical societies have been pressed for an endorsement of United Funds not only as an instrument for supporting local community services, but also supporting national health agencies, despite the fact that the policy of independent fund-raising has been firmly established by national assemblies of delegates of the American Heart Association, the American Cancer Society, and similar groups.

Fortunately for the welfare, continuing growth, and pressing need of medical research, most medical societies have resisted these attempts on the part of federated fund leadership to take financial control of the health agencies. Physicians have felt that it was important for the public to have an opportunity to give directly, without intervening authority or arbitrary allocation, to the conquest of those diseases which have affected their lives or the lives of their families. Physicians have also felt that freedom of giving is as important a public right as freedom in choice of physician.

Since federated fund leadership has been unable in most cases to pull the health agencies into fund participation through pressure on county medical societies and other community groups, some local federated funds have abandoned their historical role as fund-raising organizations, devoted to the needs of their constituent community service agencies, and are now using contributed funds to set up health programs of their own in the form of "health foundations," not affiliated with any voluntary national health agency. Once these "health foundations" are established by federated fund groups, the fund makes an appeal to the public that its "one big give" includes research and service programs on heart disease, cancer, poliomyelitis and other medical problems through its ancillary "health foundation."

In light of the resources of leadership, knowledge and experience which the Heart Association has focused since 1948 on the development of a coherent, coordinated, imaginative and professionally responsible research administrative program, which has expended a total of $29 million for medical research, it seems strange that the United Funds have felt the need to set up organizations devoted to the same purposes, simply because the health agencies

do not necessarily see matters the federated fund way.

When United Funds collect public moneys for these "foundations" as part of their drives, physicians may wish to inquire how these funds are to be administered, by what kind of board, on the basis of what experience and under the guidance of what administrative policy.

We assume that, in setting up "health foundations," United Fund leadership believes that it has valid reasons for going into programing as well as fund raising, and is not simply taking this action in administrative dudgeon at the health agencies.

We believe that health drives for national medical *research* and united funds for local community *service* can and should coexist peaceably—that the two are not necessarily mutually restrictive.

We regret that the United Funds feel the need to set up these "foundations," since we believe that the Heart Association has developed a valid program for the dispensing of funds given by the public to cope with the challenge of cardiovascular disease. However, because of the extent of that challenge, we do not wish to stand in the way of well-administered programs which scientifically and responsibly dispense funds for heart research and applied service programs.

But we do believe that the medical profession has a fundamental responsibility to see that such funds are wisely spent. My letter is to suggest criteria by means of which the medical profession can evaluate agencies such as "health foundations."

Such criteria has been established under the leadership of men like Paul Dudley White, Irvine Page and Edgar V. Allen, over the years as they formulated the operating policies and high standards of the American Heart Association. The medical profession has, I believe, an obligation to withhold both financial and advisory support from any local undertakings that do not adhere to those standards.

Sincerely yours,

HILLIARD J. KATZ, M.D.
Chairman, Public Relations Committee
California Heart Association

In Memoriam

BAER, HERMAN. Died in Elsinore, February 15, 1958, aged 78. Graduate of the Medical College of South Carolina, Charleston, 1901. Licensed in California in 1919. Doctor Baer was a retired member of the Riverside County Medical Association and the California Medical Association, and an associate member of the American Medical Association.

✤

BOURDON, EVAN COVINGTON. Died in Vallejo, January 8, 1958, aged 49, of generalized carcinomatosis due to carcinoma of the colon. Graduate of Baylor University College of Medicine, Houston, Texas, 1937. Licensed in California in 1939. Doctor Bourdon was a member of the Alameda-Contra Costa Medical Association.

✤

GAROL, HUGH W. Died in San Francisco, February 14, 1958, aged 47. Graduate of McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1938. Licensed in California in 1939. Doctor Garol was a member of the San Francisco Medical Society.

✤

GIBBONS, HENRY WALTER. Died in San Francisco, February 6, 1958, aged 80, of cor pulmonale, chronic, and chronic emphysema. Graduate of Cooper Medical College, San Francisco, 1902. Licensed in California in 1902. Doctor Gibbons was a retired member of the San Francisco Medical Society and the California Medical Association, and an associate member of the American Medical Association.

✤

JOYCE, THOMAS FRANCIS. Died February 10, 1958, aged 85. Graduate of the Bellevue Hospital Medical College, New York, N. Y., 1898. Licensed in California in 1930. Doctor Joyce was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.

✤

MCCOOL, JOSEPH LETELLE. Died in Monrovia, February 12, 1958, aged 78. Graduate of the University of Pennsylvania School of Medicine, Philadelphia, 1900. Licensed in California in 1929. Doctor McCool was a retired member of the San Francisco Medical Society and the California Medical Association, and an associate member of the American Medical Association.

✤

SCHWARTZ, SIDNEY. Died in Modesto, February 3, 1958. Graduate of Stanford University School of Medicine, Stanford-San Francisco, 1938. Licensed in California in 1938. Doctor Schwartz was a member of the Stanislaus County Medical Society.

✤

WALLACE, JOHN ASHER. Died in San Bernardino, February 4, 1958, aged 53. Graduate of the University of Colorado School of Medicine, Denver, 1930. Licensed in California in 1930. Doctor Wallace was a retired member of the San Bernardino County Medical Society and the California Medical Association, and an associate member of the American Medical Association.

✤

WALTON, ROBERT. Died February 20, 1958, aged 67. Graduate of the George Washington University School of Medicine, Washington, D. C., 1916. Licensed in California in 1930. Doctor Walton was a member of the Los Angeles County Medical Association.

APPLICATION FOR HOUSING ACCOMMODATIONS

FOR YOUR CONVENIENCE in making hotel reservations for the coming meeting of the **California Medical Association,** April 27 to 30, 1958, Los Angeles, hotels and their rates are at the right. Use the form at the bottom of this page, indicating your first and second choice. Because of the limited number of single rooms available, you will stand a much better chance of securing accommodations of your choice if your request calls for rooms to be occupied by two or more persons. **All requests for reservations must give definite date and hour of arrival as well as definite date and approximate hour of departure; also names and addresses of all occupants of hotel rooms must be included.**

ALL RESERVATIONS MUST BE RECEIVED BEFORE: APRIL 21, 1958

Eighty-seventh Annual Session
CALIFORNIA MEDICAL ASSOCIATION
Los Angeles, California
APRIL 27-30, 1958

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3355 Wilshire Boulevard	8.00	10.50	18.00
HOTEL CHANCELLOR			
3191 West Seventh Street	7.00- 8.00	10.00-12.00	
SHERATON-TOWN HOUSE			
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Please reserve the following accommodations for the 87th Annual Session of the California Medical Association, in Los Angeles April 27 to 30, 1958.

Single Room $..... Twin Bedded Room $.....

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Individual Requesting Reservations—Please print or type Delegate?..... Alternate?.....

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87th Annual Session

CALIFORNIA MEDICAL ASSOCIATION IN COOPERATION WITH THE

College of Medical Evangelists
University of California at Los Angeles and
University of Southern California

Presents . . .

Three New Postgraduate Courses During
C. M. A. Annual Session

Abdominal Pain

Program planned by the University of California at Los Angeles School of Medicine

THOMAS H. STERNBERG, M.D.
Assistant Dean for Postgraduate Medical Education
Course Chairman: SHERMAN M. MELLINKOFF, M.D.

APRIL 28, 29 and 30

West Venetian Room, Ambassador Hotel

MONDAY, APRIL 28

9:00-9:45 a.m.—**Painful Medical Diseases of the Abdomen**—William E. Molle, M.D.

9:45-10:00 a.m.—**Recess.**

10:00-10:45 a.m.—**Psychiatric Aspects of Abdominal Pain**—Frank F. Tallman, M.D.

10:45-11:30 a.m.—**Panel Discussion**—William E. Molle, M.D., Sherman M. Mellinkoff, M.D., and Frank F. Tallman, M.D.

11:30-12:00 noon—**Questions.**

TUESDAY, APRIL 29

9:00-9:45 a.m.—**Surgical Causes of Abdominal Pain**—Mark M. Ravitch, M.D.

9:45-10:00 a.m.—**Recess.**

10:00-10:45 a.m.—**Retroperitoneal Causes of Abdominal Pain**—Chester C. Winter, M.D.

10:45-11:30 a.m.—**Panel Discussion**—Chester C. Winter, M.D., Sherman M. Mellinkoff, M.D., and Mark M. Ravitch, M.D.

11:30-12:00 noon—**Questions.**

WEDNESDAY, APRIL 30

9:00-10:30 a.m.—**Systemic Causes of Abdominal Pain**—Sherman M. Mellinkoff, M.D.

10:30-10:45 a.m.—**Recess.**

10:45-11:30 a.m.—**Panel Discussion—Differential Diagnosis of Abdominal Pain**—William E. Molle, M.D., Sherman M. Mellinkoff, M.D., Mark M. Ravitch, M.D., Frank F. Tallman, M.D., and Chester C. Winter, M.D.

11:30-12:00 noon—**Questions.**

Fee: $25.00.*

*Interns and Residents with proper identification will be registered without payment of the fee.

Liver Diseases

Program planned by the University of Southern California School of Medicine

PHIL R. MANNING, M.D., *Director Postgraduate Division*
Course Director: TELFER B. REYNOLDS, M.D.

APRIL 27, 28 and 29

Ambassador Hotel and Los Angeles County General Hospital

SUNDAY, APRIL 27

Symposium on Jaundice

(Los Angeles County General Hospital)

2:00-3:00 p.m.—**Panel—Liver Function Tests:**
Telfer B. Reynolds, M.D., Moderator
Charles S. Davidson, M.D.
Bernard J. Haverback, M.D. Allan G. Redeker, M.D.

3:00-5:00 p.m.—**Clinic on Jaundice.** Small groups will see and discuss interesting patients with the faculty.

MONDAY, APRIL 28

Ambassador Hotel, French Room

9:00-9:40 a.m.—**Viral Hepatitis**—Charles S. Davidson, M.D.

9:40-10:10 a.m.—**Malignant Carcinoid Syndrome**—Bernard J. Haverback, M.D.

10:10-10:40 a.m.—**Wilson's Disease; A Treatable Condition**—Telfer B. Reynolds, M.D.

10:40-10:50 a.m.—**Recess.**

10:50-12:00 noon—**Diagnostic Techniques Applicable to Liver Disease**
Splenoportography—William P. Mikkelsen, M.D.
Hepatic Vein Catheterization—Allan G. Redeker, M.D.
Liver Biopsy—Telfer B. Reynolds, M.D.

TUESDAY, APRIL 29

Ambassador Hotel, French Room

Symposium on Cirrhosis

9:00-9:30 a.m.—**Alcohol vs. Nutrition in the Etiology of Cirrhosis**—Charles S. Davidson, M.D.

Complications of Cirrhosis

9:30-10:00 a.m.—**Ascites**—Telfer B. Reynolds, M.D.

10:00-10:40 a.m.—**Portal Hypertension**—William P. Mikkelsen, M.D., and Telfer B. Reynolds, M.D.

10:40-10:50 a.m.—**Recess.**

10:50-12:00 noon—**Hepatic Coma and Its Relationship to Ammonium Metabolism**—Charles S. Davidson, M.D.

Fee: $25.00. Limited to 100 Registrants.

Postgraduate Courses

WILLIAM A. ALTEMEIER, M.D., Christian R. Holmes Professor of Surgery, University of Cincinnati College of Medicine

CHARLES S. DAVIDSON, M.D., Associate Professor of Medicine, Harvard Medical School, Boston

MARK M. RAVITCH, M.D., Associate Professor of Surgery, Johns Hopkins University School of Medicine, Baltimore

BRONSON S. RAY, M.D., Professor of Clinical Surgery (Chief, Department of Neurosurgery), New York Hospital-Cornell University Medical College, New York City

guest speakers

Management of Trauma

Program planned by College of Medical Evangelists

HAROLD M. WALTON, M.D.
Chairman, Graduate and Postgraduate Medicine

APRIL 28, 29 and 30

Ambassador Hotel
Embassy Room—Monday and Tuesday
East Venetian Room—Wednesday

MONDAY, APRIL 28

Robert L. Marsh, M.D., Chairman and Moderator

GENERAL TOPIC

Basic Science Applications to Trauma with Particular Attention to Shock and Burns

9:00-9:15 a.m.—**Fluid and Electrolytes**—David B. Hinshaw, M.D.
9:15-9:30 a.m.—**Hemorrhage**—Harry A. Davis, M.D.
9:30-9:45 a.m.—**Vasomotor Responses**—Philip J. Vogel, M.D.
9:45-10:00 a.m.—**Endocrines**—Roy F. Perkins, M.D.
10:00-10:15 a.m.—**Ventilation**—Clarence R. Collier, M.D.
10:15-10:35 a.m.—**Discussion and Summary**—Mark M. Ravitch, M.D.
10:35-10:50 a.m.—**Recess.**
10:50-12:00 noon—**Panel Discussion**
Robert L. Marsh, M.D., Moderator

Mark M. Ravitch, M.D.	Roy F. Perkins, M.D.
Harry A. Davis, M.D.	Philip J. Vogel, M.D.
Clarence R. Collier, M.D.	David B. Hinshaw, M.D.

TUESDAY, APRIL 29

Harry C. Prout, M.D., Chairman and Moderator

GENERAL TOPIC

Injuries to the Thorax and Abdomen

9:00-9:15 a.m.—**Injuries to the Thorax**—Ellsworth E. Wareham, M.D.
9:15-9:30 a.m.—**Injuries to the Abdomen**—Harry C. Prout, M.D.
9:30-9:45 a.m.—**Injuries to Blood Vessels**—Max R. Gaspar, M.D.
9:45-10:00 a.m.—**Injuries to the Genitourinary System**—Roger W. Barnes, M.D.
10:00-10:15 a.m.—**Management of Patients with Burns**—Clifford A. Barber, M.D.
10:15-10:35 a.m.—**Discussion and Summary**—William A. Altemeier, M.D.
10:35-10:50 a.m.—**Recess.**
10:50-12:00 noon—**Panel Discussion:**
Harry C. Prout, M.D., Moderator
William A. Altemeier, M.D.

Roger W. Barnes, M.D.	Clifford A. Barber, M.D.
Max R. Gaspar, M.D.	Ellsworth E. Wareham, M.D.

WEDNESDAY, APRIL 30

Alonzo J. Neufeld, M.D., Chairman and Moderator

GENERAL TOPIC

Injuries to Nervous System, Face, Skeleto-Muscular Structures

9:00-9:20 a.m.—**Injuries to Facial Structures**—Leland R. House, M.D.
9:20-9:40 a.m.—**Mechanism of Cerebral Injuries**—Cyril B. Courville, M.D.
9:40-10:00 a.m.—**Treatment of Injuries to the Nervous System**—Bronson S. Ray, M.D.
10:00-10:20 a.m.—**Injuries to Skeleto-Muscular Structures**—Vernon L. Nickel, M.D.
10:20-10:40 a.m.—**Recess.**
10:40-12:00 noon—**Panel Discussion:**
Alonzo J. Neufeld, M.D., Moderator

Bronson S. Ray, M.D.	Leland R. House, M.D.
Cyril B. Courville, M.D.	Vernon L. Nickel, M.D.

Fee: $25.00

APPLICATION FORM

POSTGRADUATE ACTIVITIES
CALIFORNIA MEDICAL ASSOCIATION
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Enclosed please find my check for $25.00, made payable to *California Medical Association*. I plan to attend the Postgraduate Course..... in Los Angeles during the California Medical Association annual session.

Name.....

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☐ I am in General Practice
☐ I limit my practice to.....

Medical school attended.....

Year of graduation.....

Interns and Residents are invited to attend free of charge.

WOMAN'S AUXILIARY
TO THE CALIFORNIA MEDICAL ASSOCIATION

The Word from Dr. Allman

"INFORM YOUR MEMBERSHIP" has been my theme for the year. Because I too need information, I have been a faithful reader of the *Journal of the American Medical Association* and of CALIFORNIA MEDICINE. Last Sunday as I perused through the February 22 issue of the *J.A.M.A.*, I found Dr. David B. Allman's article on the Woman's Auxiliary — medicine's staunchest ally. Instantly, I thought of at least a dozen physicians that I would like to send a reprint to. Imagine my surprise when in the Monday mail I found a reprint addressed to me.

I certainly hope that every state medical association president reads it; and in particular that every county medical society president reads it. Over and over again as I visit various counties I hear that many county medical society presidents are almost unaware of the Woman's Auxiliary. This is so unfortunate, because we do our finest work for them; furthering the nurse recruitment program, contributing generously to the American Medical Education Foundation, to Physicians' Benevolence and in furthering health legislation. It is on the county level that the fresh and imaginative ideas emerge, and it is here that encouragement must come from the physicians.

I'm certain that many of you have not seen Dr. Allman's message, and so I am going to quote from it:

"I believe that our county and state medical societies should take advantage of the willingness and the talent of Woman's Auxiliaries. Tell them what they can do; tell them how they can serve the medical profession at the local level. Potential woman-power is at our command, but it is worthless if we do not release its energy.

"However, we cannot turn Woman's Auxiliaries loose without the necessary background, current information, and proper training on a specific project. The auxiliary members themselves do not want to work in a haphazard fashion. They want to understand and they want to be well-informed. In every activity in which the auxiliary can serve, we should have close coordination so auxiliary members are kept abreast of all developments. For years representatives of the auxiliary have participated in the meetings of many medical association public relations and legislation committees. I see no reason why this idea should not be expanded so that auxiliary representatives can attend most meetings of medical society committees.

"It certainly would be unwise for us to allow such a large part of medicine's great force to stand off by itself . . . we can accomplish much more if we bring the Woman's Auxiliaries closer to our state and county medical societies."

To me this is a great tribute from a great man. Are you aware that an excellent biographical article on Dr. Allman appeared in the February issue of *Current Biography?* Are you aware that Dr. Allman in his opening address at the A.M.A. meeting in Philadelphia delivered some hard-hitting words against the Forand bill, and here in California hundreds of letters have been written by auxiliary members to our congressmen and senators opposing this bill? Are you aware that the July issue of the *Journal of the Medical Society of New Jersey* carries an article entitled, David Allman, The Physician? It is considered one of the finest written tributes ever paid to a president of the American Medical Association. It was written by Dr. Maurice Bear Gordon, who served on Dr. Allman's surgical service at the Atlantic City Hospital in 1940.

Many articles and stories have appeared in the press and professional journals since Dr. Allman was inaugurated at the A.M.A. in New York. He has appeared on television and with Rabbi Martin M. Weitz discussed "How Religion and Medicine Go Hand in Hand."

This is the great gentleman who says, "It should be the duty of each state and county medical society to provide more ways for the Auxiliary member to serve the medical profession."

It has indeed been a pleasure to write this monthly article for CALIFORNIA MEDICINE. Next month will be my last contribution; and it will be my report to the House of Delegates of the California Medical Association.

MRS. LEONARD D. OFFIELD
President, Woman's Auxiliary to the California Medical Association

NEWS & NOTES

NATIONAL • STATE • COUNTY

ALAMEDA

Dr. Charles E. Smith, dean of the School of Public Health of the University of California, has been appointed to the National Advisory Council on Allergy and Infectious Diseases, a division of the National Institutes of Health. The appointment, announced by United States Surgeon General L. E. Burney, is for a period of four years ending in 1962.

LOS ANGELES

Dr. Roger O. Egeberg, formerly director of the Los Angeles County General Hospital, recently was appointed medical chief of the Los Angeles County Department of Charities. Dr. Egeberg succeeds Dr. Howard F. West, who retired from the post last October.

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Dr. George V. Webster of Pasadena was elected president of the American Society for Surgery of the Hand at the organization's recent annual meeting in New York City.

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There will be a dinner meeting of the **Harvard Medical Alumni Association** of Southern California on April 23 at 6:30 p.m. at the California Club, 538 South Flower Street in downtown Los Angeles. All graduates from the Harvard Medical School are invited to attend. Information concerning reservations may be obtained from Dr. Lowell F. Bushnell, 1321 North Vermont Avenue, Los Angeles 27.

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The Foundation of the American Society of Plastic and Reconstructive Surgery announced recently that **Dr. Bernard G. Sarnat** of Beverly Hills was the recipient of the society's senior award for 1957 for research in plastic and reconstructive surgery. Dr. Sarnat received the organization's junior award in 1950.

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The **City of Hope Medical Center** in Duarte, California, has announced that it is receiving applications for a residency and a research fellowship. The residency, the announcement said, will emphasize clinical aspects of diagnosis and treatment of heart disease and cardiac catheterization. The research fellowship will provide more detailed training in techniques of physiologic investigation of patients with cardiovascular disorders and also an opportunity for the fellow to devote approximately half his time to a research project in the animal of clinical laboratories. The residency is for a year and the salary stipend is $3,600. The fellowship is for a year and may be renewed for one additional year, with salary stipend of $4,000 to $4,800. Further information may be obtained from Dr. Max Harry Weil, City of Hope Medical Center, Duarte.

PLACER-NEVADA-SIERRA

Dr. Louis E. Jones, Roseville, who has been secretary of the California State Board of Medical Examiners since 1949, has been appointed to the executive committee of the Federation of State Boards of Medical Examiners of the United States. Dr. Jones addressed a recent convention of the Federation in Chicago.

SAN FRANCISCO

Dr. William H. Creger of the Stanford University School of Medicine has received an award of $10,235 from the American Cancer Society to support an investigation of the relationship between certain blood groups and a tendency to cancer of the stomach.

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The 1958 meeting of the **American Goiter Association** will be held in the St. Francis Hotel, San Francisco, June 17 to 19. The program of the three-day meeting, it was announced by the association, will consist of papers and discussions dealing with the physiology and diseases of the thyroid gland.

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The **American College of Angiology** has announced that its fourth annual meeting will be held June 21 and 22, 1958, at the Fairmont Hotel, San Francisco. The meeting will consist of four scientific sessions devoted to cardiovascular medicine, cerebrovascular disease and experimental angiology.

The co-chairmen are Dr. Alvin Bakst, Brooklyn, Dr. J. Earle Estes, Mayo Clinic, Dr. George P. Fulton, San Francisco, and Dr. Paul S. Lowenstein, St. Louis.

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Dr. William L. Weirich, chief resident in surgery at the University of California Medical Center in San Francisco, has been named a Markle Scholar in Medical Science, it was announced recently by the John and Mary R. Markle Foundation. The scholarship carries with it a grant of $30,000 in support of the salary and research program of the recipient over a period of five years.

Dr. Weirich's research interests, it was announced, are in cardiac surgery and physiology, including changes in circulatory function occasioned by the use of pump oxygenators.

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The Florence Crittenton Home of San Francisco, which offers **care and counsel to unwed mothers,** has announced the publication of a new brochure that is available to physicians who may wish to inform themselves as to the facilities and services of the Home.

Titled "The Girl Outside," the brochure tells of the programs for girls who are resident at the Home and of help available to girls who do not enter the Home but seek advice.

Copies of the brochure may be had by writing to the Florence Crittenton Home, Broderick and Golden Gate Avenue, San Francisco 15. The telephone number is JOrdan 7-6720.

GENERAL

Dr. James F. Regan, Glendale, and **Dr. George S. Johnson** of the Stanford University School of Medicine, San Francisco, have been appointed to the California State Board of Medical Examiners by Governor Goodwin Knight for terms ending in 1962. They succeed Dr. William F. Quinn of Los Angeles and Dr. Henry Gibbons III of San Francisco.

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Mainland physicians have been invited by the Hawaii Medical Association to attend the **Hawaii Summer Medical Conference** in Honolulu July 1 to 3, 1958. The conference has been timed to follow soon after the annual

meeting of the American Medical Association which is to be held in San Francisco June 23 to 27.

Included in the program of the conference are breakfast panels and a special afternoon clinic at a Honolulu hospital.

The announcement said that additional information or arrangements for reservations may be obtained by writing to Lee Kirkland Travel, care of Medical Tours, Postoffice Box 3433, Chicago 54, Illinois.

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Dr. H. Spencer Hoyt of Monterey was installed as president of the western section of the American Urological Association at the association's convention held recently at Palm Springs, California. Dr. Hoyt succeeds Dr. Lyle G. Craig of Pasadena. Dr. Charles M. Stewart of Los Angeles was reelected secretary-treasurer.

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The western regional meeting of the **International College of Surgeons** will be held in Reno, August 21 to 23, at the Riverside Hotel. Further information may be obtained from Dr. Leo D. Nannini, 190 Mill Street, Reno, Nevada.

POSTGRADUATE EDUCATION NOTICES

THIS BULLETIN of the dates of postgraduate education programs and the meetings of various medical organizations in California is supplied by the Committee on Postgraduate Activities of the California Medical Association. In order that they may be listed here, please send communications relating to your future medical or surgical programs to: Mrs. Margaret H. Griffith, Director, Postgraduate Activities, California Medical Association, 2975 Wilshire Boulevard, Los Angeles 5.

UNIVERSITY OF CALIFORNIA AT LOS ANGELES

Proctology. Wednesday, April 16. Six hours.†

Medical Technology Workshop: Microbiology. Saturday and Sunday, April 19 and 20. Six hours. Fee: $8.00.

Dermatology in General Practice (enrollment limited). Wednesdays, April 23 to May 28. Twelve hours. Fee: $50.00.

Advances in Behavioral Science of Significance for Rehabilitation. Saturday, April 26. Seven hours. Fee: $10.00.

Casts, Splints and Bandages (enrollment limited). Wednesday, May 7 (inclusive). Six hours. Fee: $40.00.

Collagen Diseases. Friday and Saturday, May 23 and 24. Nine hours. Fee: $35.00.

Emotional Problems in Office Practice (University of California Residential Conference Center, Lake Arrowhead). Thursday through Saturday, June 5 to 7. Sixteen hours. Fee: $150.00 (including room and meals).

Seventh Annual Symposium on Medical Technology. Saturday and Sunday, June 14 and 15. Twelve hours. Fee: $20.00.

†Fee to be announced.

Techniques of Hypnosis (enrollment limited). Monday through Wednesday, June 16 to 18. Fifteen hours. Fee: $65.00.

Advanced Techniques and Application of Hypnosis (enrollment limited). Wednesday through Friday, June 18 to 20. Fifteen hours. Fee: $110.00.

Dissection of the Thorax, Abdomen and Pelvis (enrollment limited to 32). Friday and Saturday, June 27 and 28. Twelve hours. Fee: $125.00.

Obstetrics and Gynecology. Thursday through Saturday, July 17 through July 19. Sixteen hours.†

Techniques of Surgery. Monday through Friday (limited to 14), July 28 to August 1. Forty hours: Fee: $500.00.

Internal Medicine (at University of California Residential Conference Center, Lake Arrowhead), Wednesday through Saturday, August 20 to 23. Sixteen hours.†

Anesthesiology. Wednesday through Friday, August 27 through August 29. Sixteen hours.†

Contact: Thomas H. Sternberg, M.D., Assistant Dean for Postgraduate Medical Education, U.C.L.A., Los Angeles 24. BRadshaw 2-8911, Ext. 202.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Interpretation of Laboratory Tests. Wednesday to Friday, May 14 to 16. Twenty-one hours.†

Orthopedic Surgery and Fractures. Friday and Saturday, May 16 and 17. Fourteen hours.†

Ear-Nose-Throat. Friday and Saturday, June 6 and 7. Fourteen hours. Fee: $40.00.

Fundamental Principles of Radioactivity and the Diagnostic and Therapeutic Uses of Radioisotopes. Two or three month course limited to one enrollee per month. Per month, $250.00.

Contact: Seymour M. Farber, M.D., Head, Postgraduate Instruction, Office of Medical Extension, University of California Medical Center, San Francisco 22. MOntrose 4-3600, Ext. 665.

STANFORD UNIVERSITY SCHOOL OF MEDICINE

Morning Clinical Conferences, each Monday, Room 515. *Contact:* D. H. Pischel, M.D., Professor, Division of Ophthalmology, Stanford University School of Medicine, 2398 Sacramento St., San Francisco 15.

UNIVERSITY OF SOUTHERN CALIFORNIA, LOS ANGELES

Cardiac Resuscitation. Sponsored by the Los Angeles County Heart Association each Wednesday throughout the year, 4 to 6 p.m., USC Medical Research Building, Room 211, 2025 Zonal Avenue. Residents and interns of Los Angeles County, and all armed forces medical personnel admitted without fee. Tuition for all other physicians $30.00. (Each session all-inclusive.)

Basic Home Course in Electrocardiography. One year Postgraduate Series, electrocardiogram interpretation by mail. Physicians may register at any time and receive all 52 issues. Fifty-two weeks. Fee: $100.00.

Advance Home Course in Electrocardiography. One year postgraduate series, electrocardiogram interpretation by mail. Fifty-two issues: $85.00. Physicians may register at any time.

Problems of Malpractice. Lectures will be presented on problems relating to malpractice situation in California, May 17, Hotel Statler, Los Angeles. Tuition: $18.00.

Office Orthopedics in General Practice. Designed to be of value to the physician in general practice. May 23 to 25, Hotel Statler, Los Angeles, 9 to 5 each day. Fee: $75.00.

Special Announcement: From August 5 to August 21, 1958, the University of Southern California School of Medicine will hold a postgraduate course in Honolulu and on board the *S.S. Matsonia*. The course will center around actual case histories, which will be used to emphasize diagnostic and therapeutic features.

Contact: Phil R. Manning, M.D., Director, Postgraduate Division, University of Southern California School of Medicine, 2025 Zonal Avenue, Los Angeles 33. CApital 5-1511.

COLLEGE OF MEDICAL EVANGELISTS

Audio-Visual Postgraduate Refresher Courses. Courses are made up of four or more half-hour lectures each, recorded on hi-fi magnetic tape and illustrated by 35-mm. filmstrips or slides in full color, and adapted for use on any standard tape recorder and filmstrip or slide projector, automatic or manual.

Contact: Paul D. Foster, M.D., chairman, Committee on Audio-Visual Courses, College of Medical Evangelists School of Medicine, 316 North Bailey St., Los Angeles 33.

CALIFORNIA MEDICAL ASSOCIATION POSTGRADUATE COURSES

POSTGRADUATE INSTITUTES—1958

Postgraduate Courses during California Medical Association Annual Meeting

Abdominal Pain. Program by U.C.L.A. School of Medicine. April 28, 29, 30, 9:00-12:00 a.m. Ambassador Hotel, Los Angeles.

Management of Trauma. Program by College of Medical Evangelists. April 28, 29, 30, 9:00-12:00 a.m. Ambassador Hotel, Los Angeles.

Liver Diseases. Program by U.S.C. School of Medicine. April 27, 2:00-5:00 p.m., Los Angeles County General Hospital, and April 28-29, 9:00-12:00 a.m., Ambassador Hotel, Los Angeles.

Guest Speakers: William A. Altemeier, M.D., University of Cincinnati School of Medicine; Charles S. Davidson, M.D., Harvard Medical School; Mark M. Ravitch, M.D., Johns Hopkins University School of Medicine; Bronson S. Ray, M.D., Cornell University Medical College.

Fee: $25.00 each course

For additional information and complete program write: Postgraduate Activities, California Medical Association, 2975 Wilshire Boulevard, Los Angeles 5.

AUDIO DIGEST FOUNDATION, a nonprofit subsidiary of the C.M.A., now offers (on a subscription basis) a series of hour-long tape recordings designed to keep the physician abreast of current happenings in his particular field. Composed of practice-useful abstracts from 600 leading journals, with short lectures and editorial comments from prominent physicians, Audio Digest offers programs covering general practice, surgery, internal medicine, obstetrics and gynecology, and pediatrics.

Contact: Claron L. Oakley, editor, 1919 Wilshire Blvd., Los Angeles 57.

Medical Dates Bulletin

APRIL MEETINGS

AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS, April 21 to 23, Hotel Statler, Los Angeles. *Contact:* Keith P. Russell, M.D., 511 S. Bonnie Brae, Los Angeles 5.

CANCER COMMISSION, CALIFORNIA MEDICAL ASSOCIATION CANCER CONFERENCE for Mendocino-Lake County Medical Societies, April 24, State Hospital, Ukiah.*

AMERICAN COLLEGE OF CHEST PHYSICIANS, California Chapter, Scientific Meeting, April 26, 9 to 5, Embassy Room, Ambassador Hotel, Los Angeles. *Contact:* Thomas B. Wiper, M.D., secretary-treasurer, 536 Mason Street, San Francisco 2.

AMERICAN SOCIETY OF INTERNAL MEDICINE Annual Meeting, Chalfonte-Haddon Hall, Atlantic City, April 26 and 27. *Contact:* Mrs. Mildred B. Coleman, assistant secretary, or Claude P. Callaway, M.D., secretary-treasurer, 350 Post Street, San Francisco.

CANCER COMMISSION, CALIFORNIA MEDICAL ASSOCIATION PRE-CONVENTION CONFERENCES on Pathology and Radiology, April 26, Ambassador Hotel, Los Angeles.*

CALIFORNIA MEDICAL ASSOCIATION Annual Meeting, Ambassador Hotel, Los Angeles, April 27 to 30. *Contact:* John Hunton, executive secretary, 450 Sutter St., San Francisco 8, or Ed Clancy, director, Public Relations, 2975 Wilshire Blvd., Los Angeles 5.

MAY MEETINGS

LOS ANGELES COUNTY HEART ASSOCIATION Annual Membership Meeting, May 1, 7:00 p.m., Los Angeles. *Contact:* Chauncey A. Alexander, executive director, 660 S. Western Avenue, Los Angeles 5.

CALIFORNIA CONFERENCE OF LOCAL HEALTH OFFICERS Semi-Annual Meeting, Los Angeles, May 1 and 2. *Contact:* Dr. John C. Dement, chief, Division of Local Health Service, State Department of Public Health, 2151 Berkeley Way, Berkeley 4.

HAWAII MEDICAL ASSOCIATION Annual Meeting, May 1 through May 3, Honolulu. *Contact:* Lee McCaslin, executive secretary, Hawaii Medical Association, 510 S. Beretania St., Honolulu.

**Contact:* Walter E. Batchelder, M.D., medical director, California Medical Association Cancer Commission, 450 Sutter St., San Francisco 8.

WESTERN GERONTOLOGICAL SOCIETY Third Annual Convention, May 3 and 4, Hotel Statler, Los Angeles. Begins 1:00 p.m. May 3. *Contact:* Chas. A. Preuss, M.D., president, 1317 Santa Barbara Street, Santa Barbara.

GROUP PSYCHOTHERAPY ASSOCIATION OF SOUTHERN CALIFORNIA Annual Meeting, May 3, all day, Chapman Park Hotel, Los Angeles. *Contact:* E. Parl Welch, Ph.D., 450 N. Bedford Drive, Beverly Hills.

CANCER COMMISSION, CALIFORNIA MEDICAL ASSOCIATION CANCER CONFERENCE for Sonoma County Medical Society, Santa Rosa, May 8.*

AMERICAN PSYCHIATRIC ASSOCIATION Annual Meeting, May 12 to 16, Civic Auditorium, San Francisco. *Contact:* Alfred Auerback, M.D., 450 Sutter St., San Francisco.

CHILDREN'S HOSPITAL OF THE EAST BAY Sixth Annual Clifford D. Sweet Seminar, May 16 and 17, Claremont Hotel, Berkeley. *Contact:* Arthur Bolter, M.D., Clifford D. Sweet Lectureship Committee, Children's Hospital of the East Bay, 51st and Dover St., Oakland 9.

AMERICAN ACADEMY OF APPLIED NUTRITION 22nd Annual National Convention, May 16 through May 18, Huntington-Sheraton Hotel, Pasadena. *Contact:* R. T. Pottenger, M.D., vice-president, 960 E. Green St., Pasadena.

HAWAIIAN DIVISIONAL MEETING, AMERICAN PSYCHIATRIC ASSOCIATION, May 17 to 22, Hawaiian Village, Honolulu. *Contact:* Alfred Auerback, M.D., 450 Sutter St., San Francisco.

WESTERN BRANCH, AMERICAN PUBLIC HEALTH ASSOCIATION Annual Meeting with Canadian Public Health Association, May 19 to 23, Vancouver, B. C. *Contact:* Mrs. L. Amy Darter, secretary-treasurer, 2151 Berkeley Way, Berkeley 4.

AMERICAN LARYNGOLOGICAL ASSOCIATION, May 19 to 20, San Francisco. *Contact:* James H. Maxwell, M.D., secretary, University Hospital, Ann Arbor, Michigan.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION, May 21 to 23, San Francisco. *Contact:* F. Johnson Putney, M.D., secretary, 1719 Rittenhouse Square, Philadelphia, Pa.

CALIFORNIA HEART ASSOCIATION Annual Meeting, Scientific Session and Directors Meeting, Hacienda Motel, Fresno, May 23 to 25. *Contact:* J. Keith Thwaites, executive director, 1428 Bush St., San Francisco.

SUMMER AND FALL MEETINGS

AMERICAN COLLEGE OF CHEST PHYSICIANS 24th Annual Meeting, June 18 to 22, San Francisco. *Contact:* Mr. Murray Kornfeld, executive director, 112 East Chestnut St., Chicago 11, Ill.

AMERICAN MEDICAL ASSOCIATION Annual Meeting, June 23 to 27, San Francisco. *Contact:* American Medical Association, 535 North Dearborn St., Chicago 10.

AMERICAN PROCTOLOGIC SOCIETY, June 29 to July 3, Los Angeles. *Contact:* Norman D. Nigro, M.D., secretary, 10 Peterboro St., Detroit 1, Michigan.

HAWAII MEDICAL ASSOCIATION Summer Conference, July 1 through July 3, Honolulu. *Contact:* Lee McCaslin, executive secretary, 510 S. Beretania St., Honolulu.

IDAHO STATE MEDICAL ASSOCIATION Annual Convention, July 6 to 9, Sun Valley, Idaho. *Contact:* Armand L. Bird, executive secretary, 364 Sonna Building, Boise.

ROCKY MOUNTAIN CANCER CONFERENCE, July 9 and 10, Shirley-Savoy Hotel, Denver. *Contact:* Alexis E. Lubchenco, M.D., 835 Republic Bldg., Denver 2, Colo.

NEW MEXICO CHAPTER ACADEMY OF GENERAL PRACTICE Ruidosa Summer Clinic, July 21 through July 24, Ruidosa, New Mexico. *Contact:* Frederick R. Brown, M.D., secretary-treasurer, 207 N. Union, Roswell, New Mexico.

SAINT JOHN'S HOSPITAL POSTGRADUATE ASSEMBLY, September 11 through September 14, Saint John's Hospital, Santa Monica. *Contact:* John C. Eagan, M.D., director, Postgraduate Assembly, 22nd St. at Santa Monica Blvd., Santa Monica.

WASHINGTON STATE MEDICAL ASSOCIATION Annual Convention, September 14 to 17, 1958, Spokane, Washington. *Contact:* Ralph W. Neill, executive secretary, 1309 Seventh Ave., Seattle, Wash.

NEVADA STATE MEDICAL ASSOCIATION Annual Meeting, September 17 through 20, Elko, Nevada. *Contact:* Nelson B. Neff, executive secretary, P. O. Box 188, Reno.

COLORADO STATE MEDICAL SOCIETY Annual Session, September 24 through 27, Broadmoor Hotel, Colorado Springs. *Contact:* Harvey T. Sethman, executive secretary, 835 Republic Bldg., Denver 2.

CALIFORNIA ACADEMY OF GENERAL PRACTICE Tenth Annual Scientific Assembly, October 5 to 8, Masonic Temple, San Francisco. *Contact:* William W. Rogers, executive secretary, 461 Market Street, San Francisco 5.

LOS ANGELES COUNTY HEART ASSOCIATION Professional Symposium, October 8 and 9, Wilshire Ebell Theatre, 9 to 5. *Contact:* C. A. Alexander, executive director, Los Angeles County Heart Association, 660 S. Western Avenue, Los Angeles 5.

CALIFORNIA SOCIETY OF INTERNAL MEDICINE Annual Meeting, October 17 to 19, Ahwahnee Hotel, Yosemite. *Contact:* Mrs. Mildred B. Coleman, executive secretary, or Dr. Clyde C. Greene, secretary-treasurer, 350 Post St., San Francisco 8.

AMERICAN HEART ASSOCIATION Scientific Sessions and Meetings, October 24 to 28, Fairmont Hotel and Civic Auditorium, San Francisco. *Contact:* J. Keith Thwaites, executive director, California Heart Association, 1428 Bush Street, San Francisco 9.

LOS ANGELES COUNTY HEART ASSOCIATION 28th Annual Professional Symposium, October 29 and 30, Wilshire Ebell Theater. *Contact:* Los Angeles County Heart Association, 660 S. Western Ave., Los Angeles 5, DUnkirk 5-4231.

THE PHYSICIAN'S *Bookshelf*

EMOTIONAL ILLNESS: HOW FAMILIES CAN HELP—Karl R. Beutner, M.D., and Nathan G. Hale, Jr., M.A. G. P. Putnam's Sons, 210 Madison Ave., New York City, 1957. 158 pages, $2.75.

No disease is more feared—or misunderstood—than mental illness. This small book, written to help the family of an emotionally sick patient recognize and cope with the difficulties involved, deals with one facet of the problem.

The authors discuss many types of mental functioning and behavior in the individual from common, only slightly abnormal incidents, to psychiatric emergencies. They lay emphasis on early signs and roots of mental disorders and the patient's need for medical care. They explain how the relatives can make things easier for themselves as well as for the patient. They tell what to do and how to go about getting help. On the whole, this consists of advice to consult the family doctor or proper community health agencies.

The book gives a number of points on "how to do what" when the patient and the relatives are under proper psychiatric care. It leaves unanswered the problems involved when the patient does not place himself under proper therapy. And many of the cases leave the reader dangling as to their follow-up.

In summary, the reader is told that psychotherapy is a way of dealing with human feelings through a relationship with a skilled, highly trained specialist. It is perhaps the most effective method now available to treat the kinds of problems that cause emotional illness.

The book contributes to general enlightenment about emotional illness and should be useful to the patients of general practitioners and psychiatrists alike. It should help families and perhaps patients themselves to perceive mental illness and psychiatry as one area in medicine.

EDGAR WAYBURN, M.D.

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MANUAL OF PEDIATRIC PHYSICAL DIAGNOSIS—Lewis A. Barness, M.D., Associate Professor of Pediatrics, University of Pennsylvania School of Medicine, The Year Book Publishers, Inc., 200 East Illinois, Chicago, 1957. 195 pages, $4.00.

This book is an encyclopedia of what may be seen, felt, measured and heard in the physical examination of the infant and child. It is divided into nine chapters which cover each region of the body. One chapter is given over to the examination of the newborn. There are two appendices. One is a "Record of Physical Examination" which is a recapitulation of conditions underscored in the text. The other is "Some Rare Syndromes with Characteristic Appearance." The index tabulates very well the material in the text.

In each chapter every condition, normal or abnormal, that may be present in the section of the body to be observed is mentioned and underscored. Methods of examination are also discussed.

The book is a detailed guide for the medical student, intern and resident who would make himself familiar with all conditions, normal and abnormal, that must be noted in the complete physical examination of the child, thus leading to a proper diagnosis.

For the physician in general practice or the pediatrician, the book would be one of reference. But even for them new tricks in the physical diagnosis might be learned.

E. EARL MOODY, M.D.

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MODERN PERINATAL CARE—Leslie V. Dill, M.D., F.A.C.S., Associate Clinical Professor, Obstetrics and Gynecology, Georgetown University School of Medicine. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, N. Y., 1957. 309 pages, $6.50.

This volume is designed chiefly for the practicing obstetrician, but will be found useful to the pediatrician and general practitioner as well.

The chapters devoted to Nutrition and Pregnancy, the Psychology of Pregnancy, Anemias of Pregnancy, Pregnancy and Diabetes, Fetal and Neonatal Mortality, Erythroblastosis and Breast Feeding are examples of areas in which there is great overlapping of interest on the part of pediatricians and obstetricians. The author has a readable clear style—has made generous use of easily understood diagrams and has followed each chapter with a particularly generous and up-to-date list of references.

The book can be recommended to physicians caring for newborns and as an addition to a modern newborn nursery library.

W. DEAMER, M.D.

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CHEMISTRY AND BIOLOGY OF PURINES—Ciba Foundation Symposium—G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Cecilia M. O'Connor, B.Sc., Editors for the Ciba Foundation. Little, Brown and Company, Boston, 1957. 327 pages, 124 illustrations, $9.00.

In these days of nuclear and cellular research, the twenty-two lectures, given by leading workers in most of the countries of the British Commonwealth and the United States of America are of great interest, especially to those interested in the biology of cancer and in cellular metabolism. The lectures are related only in that they discuss various aspects of the structure and metabolism of purine derivatives; otherwise there is no connecting thread and the book is not intended for the beginning student. Rather, the lectures were given by experts to experts at the Ciba Foundation Symposium held on the 8th to 10th of May, 1956 in London. A few titles, selected at random, are "Synthesis and properties of purines of potential biological interest," "The π-electron properties of purines calculated by the L. C. A. O. method," "Stereochemistry of nucleoside synthesis," "Biological and microbiological activity of purine analogues of vitamin B_{12}," "The use of 6-mercaptopurine in the treatment of leukemia," "Enzymic control of purines by xanthine oxidase."

C. H. THIENES, M.D.

ORTHOPEDICS FOR THE GENERAL PRACTITIONER—William E. Kenney, M.D., Orthopedic Surgeon, Truesdale Hospital; and Carroll B. Larson, M.D., F.A.C.S., Professor of Orthopedic Surgery and Chairman of Department of Orthopedic Surgery, State University of Iowa. The C. V. Mosby Company, St. Louis, 1957. 413 pages, $11.50.

This new book should be available to, or in the library of all physicians concerned with diseases and disorders of the bones, joints, and muscles.

Each of the fourteen chapters is organized to diagnose and treat specific problems, from congenital defects of the newborn to neoplasms of bone. An excellent outline of symptoms and their most likely cause precedes each new subject. This feature makes quick reference easy. The one hundred and eighty illustrations are sharp, clear, and free of distracting, extraneous matter.

The pertinent roentgenograms are clearly reproduced. Helpful estimates of disability periods follow sections on injuries. A refreshing minimum of footnotes, references, and statistical tables, combined with the clear, sharp type makes easy, pleasant reading. Controversial subjects are discussed with tact and restraint.

The critical reader should forgive the occasional error in spelling and the frequent use of trade names for common drugs.

This book is sincerely recommended to the general practitioner and pediatrician. Interns and residents should find it especially helpful. As the authors say in the preface, "by using this book a doctor should be able to arrive at a diagnosis and outline his treatment with a minimum loss of time."

JAMES E. REEVES, M.D.

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PROGRESS IN NEUROLOGY AND PSYCHIATRY—An Annual Review—Volume XII—Edited by E. A. Spiegel, M.D., Professor and Head of the Department of Experimental Neurology, Temple University School of Medicine, Grune & Stratton, New York, 1957. 657 pages, $12.00.

This annual volume continues to be of tremendous value to neurologists, psychiatrists, and those working in related fields, providing as it does essentially an annotated bibliography of work published the previous year. It is doubtful if anyone reads the book through, but in addition to supplying a summary of progress in fields of immediate interest to the physician it remains as a bibliography capable of saving much time and effort when a particular subject wants investigation. As is always the case in such a book which is the joint effort of a number of authors, the excellence of coverage varies widely from chapter to chapter, but in the main is quite adequate. Although it is aimed at the specialist, it should make interesting reading for anyone interested in nervous function.

HENRY NEWMAN, M.D.

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ALCOHOLISM—A Treatment Guide for General Practitioners—Donald W. Hewitt, M.D., Lea & Febiger, Philadelphia, 1957. 112 pages, $3.00.

This small book of about 100 pages has as its avowed objective the dissemination of knowledge regarding the nature and treatment of alcoholism to the general practitioner. The presentation of the facts is generally sound, and the practical suggestions as to how to deal with the different varieties of chronic alcoholism should be helpful to the physician who has to meet this problem in his practice. The crux of the situation is, however, the lack of enthusiasm of the profession as a whole to accept such individuals as patients. As a result, although the more affluent may be under the observation of a psychiatrist early in their illness, the rank and file of alcoholics receive medical attention only after years of abuse of the drug result in tangible evidence of organic brain and nerve involvement. Perhaps the reluctance of the practitioner to assume the care of these unfortunate individuals springs from the generally recognized poor prognosis of this type of addiction, perhaps equally from the generally held concept of alcoholism as a form of vice rather than illness. For those general practitioners who are willing to assume the obligation of treating alcoholics as sick people, this book should prove valuable. For the specialist in the field, it will reveal little not already known.

HENRY NEWMAN, M.D.

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ATOMIC ENERGY IN MEDICINE—K. E. Halnan, M.D. (Atoms for Peace Series, D. W. Morley, ed.), Philosophical Library, Inc., 15 East 40th Street, New York 16, N. Y., 1957. 157 pages, tables, illustrations and 14 plates, $6.00.

The author states in the foreword that this book is written for the layman and the professional worker in the field of atomic energy in medicine. The book is such easy reading and so well written, obviously written by a man who has been close to the field of atomic energy and medicine for a long time, that it seems to me it would be worth while reading for practically anyone interested in the field. The common sense, practical, down to earth discussion of atomic energy in medicine makes this book valuable.

The chapters are: (1) Introduction to atomic physics and the nuclear reactor; (2) The principles of use of radioactive isotopes; (3) Radioactive isotopes in medical research; (4) Radiobiology; (5) Cancer and radiotherapy; (6) Radioactive iodine and the thyroid gland; (7) Radioactive isotopes and blood diseases; (8) Other new aids to diagnosis; (9) The medical use of high energy particle accelerators; (10) Problems and hazards of radiation; (11) The future.

JOHN H. LAWRENCE, M.D.

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CRAIG AND FAUST'S CLINICAL PARASITOLOGY—Sixth Edition—Ernest Carroll Faust, A.B., M.A., Ph.D., William Vincent Professor of Tropical Diseases and Hygiene, Tulane University School of Medicine; and Paul Farr Russell, M.D., M.P.H., Staff Member, The Rockefeller Foundation; Consultant to Surgeon General, U. S. Army. Lea & Febiger, Philadelphia, 1957. 1078 pages, 346 illustrations, 7 colored plates, $15.00.

A new and revised sixth edition of a standard textbook has appeared twenty years after the introduction of the first edition. The junior author of the previous editions becomes the senior author, and the new junior author, Dr. Paul Farr Russell, is a world authority in the field of Tropical Public Health, with emphasis on malariology.

Basically the text is organized in a manner similar to previous editions, but several new subjects such as visceral larval migrans and alveolar hydatid disease have been added. The treatment of parasitic infections has been brought up-to-date; the treatment schedules are compiled in a table in the front of the book, a table that is particularly useful to clinicians.

Clinical Parasitology, although of primary value to advanced students of parasitology, is extremely useful for clinicians seeking information about geographical distribution, symptomatology, and laboratory procedures to establish the diagnosis of parasitic infections. The technical appendix contains valuable information on the proper collection of specimens for laboratory examination and identification.

This text is recommended as a reference, particularly for clinicians on the Pacific Coast, because of the higher frequency of parasitic infections seen in a population containing a higher percentage of Orientals and migrant laborers of foreign origin.

QUENTIN M. GEIMAN, Ph.D.